EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S1	836	"562/450".CCLS.	US-PGPUB; USPAT; USOCR	OR	ON	2007/05/02 12:36
S2	295	S1 and @ad<="20020311"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/05/02 17:08
S3	44	((PAUL) near2 (SUTTON)).INV.	US-PGPUB; USPAT; USOCR	OR	ON	2007/05/02 12:37
S4	10	((RICHARD) near2 (VIVILECCHIA)).INV.	US-PGPUB; USPAT; USOCR	OR	ON	2007/05/02 12:38
S5	366	((DAVID) near2 (PARKER)).INV.	US-PGPUB; USPAT; USOCR	OR	ON	2007/05/02 12:38
S6	1	((MARILYN) near2 ("DE LA CRUZ")).INV.	US-PGPUB; USPAT; USOCR	OR	ON	2007/05/02 12:38
S7	1	("5463116").PN.	US-PGPUB; USPAT	OR	OFF	2007/05/02 12:48
S8	0	EP-0526171-$.did.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/05/02 12:48
S9	2	EP-526171-$.did.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/05/02 12:51
S10	0	WO-0126639-$.did.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/05/02 12:49
S11	1	WO-200126639-$.did.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/05/02 13:14
S12	1	("4816484").PN.	US-PGPUB; USPAT	OR	OFF	2007/05/02 12:51
S13	0	EP-0196222-$.did.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/05/02 12:51

EAST Search History

S14	1	EP-196222-$.did.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/05/02 12:51
S16	987	(562/444,445).CCLS.	US-PGPUB; USPAT; USOCR	OR	OFF	2007/05/02 13:15
S17	585	S16 and @ad<="20020311"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/05/02 13:22
S18	29	nateglinide.clm. and @ad<="20020311"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/05/02 13:32
S19	3	("6559188").URPN.	USPAT	OR	ON	2007/05/02 13:25
S20	0	("6878749").URPN.	USPAT	OR	ON	2007/05/02 13:28
S21	0	("6949555").URPN.	USPAT	OR	ON	2007/05/02 13:29
S22	262	nateglinide.clm. or repaglinide. clm. and @ad<="20020311"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/05/02 13:30
S23	0	"nateglinide.clm. or repaglinide. clm." and @ad<="20020311"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/05/02 13:31
S24	0	"salts of nateglinide.clm." and @ad<="20020311"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/05/02 13:31
S25	0	"salts of nateglinide"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/05/02 13:31
S26	0	"salt of nateglinide"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/05/02 14:32
S27	46	salt adj5 nateglinide	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/05/02 13:32
S28	5	S27 and @ad<="20020311"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/05/02 14:33
S29	3	("2001/0016586").URPN.	USPAT	OR	ON	2007/05/02 13:33

EAST Search History

S30	0	("2006/0004102").URPN.	USPAT	OR	ON	2007/05/02 14:12
S31	0	("2007/0043117").URPN.	USPAT	OR	ON	2007/05/02 14:31
S32	358	nateglinide adj5 repaglinide	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/05/02 14:33
S33	45	S32 and @ad<="20020311"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/05/02 14:51
S34	0	WO-03076393-$.did.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/05/02 14:51
S35	1	WO-2003076393-$.did.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/05/02 14:51
S36	1462	"514/563".CCLS.	US-PGPUB; USPAT; USOCR	OR	ON	2007/05/02 17:05
S37	836	"562/450".CCLS.	US-PGPUB; USPAT; USOCR	OR	ON	2007/05/02 17:06
S38	617	"514/62".CCLS.	US-PGPUB; USPAT; USOCR	OR	ON	2007/05/02 17:07
S39	512	"536/55.3".CCLS.	US-PGPUB; USPAT; USOCR	OR	ON	2007/05/02 17:08
S40	792	S36 and @ad<="20020311"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/05/02 17:08
S41	295	S37 and @ad<="20020311"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/05/02 17:09
S42	359	S38 and @ad<="20020311"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/05/02 17:09
S43	320	S39 and @ad<="20020311"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/05/02 17:09

10/507255 SALTS OF NATEGLINIDE -str_regno_text -Search

=> d his

(FILE 'HOME' ENTERED AT 17:49:04 ON 02 MAY 2007)

FILE 'REGISTRY' ENTERED AT 17:49:18 ON 02 MAY 2007
L1 STRUCTURE UPLOADED
L2 5 S L1 SSS SAM
L3 82 S L1 SSS FULL

FILE 'HCAPLUS' ENTERED AT 17:50:19 ON 02 MAY 2007
L4 44 S L3/P
L5 14 S SALT? AND L4
E US20050234129/PRN,PN,AN
E US200500234129/PRN,PN,AN
E NATEGLINIDE+ALL/CT
L6 0 S SALT? (W) NATEGLINIDE
L7 1 S "NATEGLINIDE SALT?"
E US2005234129/PRN,PN,AN

FILE 'STNGUIDE' ENTERED AT 18:00:24 ON 02 MAY 2007
L8 0 S 105816-04-4/RN OR 592523-31-4/RN OR 592523-32-5/RN OR 592524

FILE 'REGISTRY' ENTERED AT 18:04:27 ON 02 MAY 2007
L9 9 S 105816-04-4/RN OR 592523-31-4/RN OR 592523-32-5/RN OR 592524

FILE 'STNGUIDE' ENTERED AT 18:06:38 ON 02 MAY 2007

FILE 'HCAPLUS' ENTERED AT 18:07:36 ON 02 MAY 2007

FILE 'STNGUIDE' ENTERED AT 18:08:42 ON 02 MAY 2007

FILE 'HCAPLUS' ENTERED AT 18:14:39 ON 02 MAY 2007

FILE 'REGISTRY' ENTERED AT 18:14:56 ON 02 MAY 2007
L10 0 S 105816-04-4/PRO

FILE 'CASREACT' ENTERED AT 18:15:57 ON 02 MAY 2007
L11 13 S 105816-04-4/PRO

=> file casreact
COST IN U.S. DOLLARS — SINCE FILE ENTRY: 0.90 — TOTAL SESSION: 416.59
FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) — SINCE FILE ENTRY: 0.00 — TOTAL SESSION: -46.02
CA SUBSCRIBER PRICE

FILE 'CASREACT' ENTERED AT 18:15:57 ON 02 MAY 2007
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FILE CONTENT:1840 - 29 Apr 2007 VOL 146 ISS 19

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* CASREACT now has more than 12 million reactions *
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Some CASREACT records are derived from the ZIC/VINITI database (1974-1999) provided by InfoChem, INPI data prior to 1986, and Biotransformations database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 105816-04-4/pro
L11 13 105816-04-4/PRO

=> d l11 ibib abs

L11 ANSWER 1 OF 13 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 146:163387 CASREACT
TITLE: Preparation of H type nateglinide crystal
INVENTOR(S): Chen, Songnian; Feng, Qianjian; Yu, Yingmin
PATENT ASSIGNEE(S): Hangzhou Pollen Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 5pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1887858	A	20070103	CN 2006-10052617	20060721

PRIORITY APPLN. INFO.: CN 2006-10052617 20060721
AB The title method comprises the steps of: (1) condensing trans-4-isopropylcyclohexanecarbonylchloride with D-phenylalanine to obtain crude crystal of B type nateglinide, (2) dissolving the crude crystal in the solution of methanol, aminomethane and water (volume ratio of 60:20:20), heating to 40-60°C, adding 2% active carbon, decoloring for 7-15 min, filtrating, cooling to 10°C to precipitate, filtrating, washing with 40% ethanol till neutral, and drying to obtain H type nateglinide crystal, and (3) recrystg. the mother solution to obtain H type nateglinide crystal. The product of H type nateglinide crystal has good physiol. activity.

trans-4-isopropylcyclohexanecarbonylchloride with D-phenylalanine to obtain crude crystal of B type nateglinide, (2) dissolving the crude crystal in the solution of methanol, aminomethane and water (volume ratio of 60:20:20), heating to 40-60°C, adding 2% active carbon, decoloring for 7-15 min, filtrating, cooling to 10°C to precipitate, filtrating, washing with 40% ethanol till neutral, and drying to obtain H type nateglinide crystal, and (3) recrystg. the mother solution to obtain H type nateglinide crystal. The product of H type nateglinide crystal has good physiol. activity.

=> d l11 ibib abs 1-13

L11 ANSWER 1 OF 13 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 146:163387 CASREACT
TITLE: Preparation of H type nateglinide crystal
INVENTOR(S): Chen, Songnian; Feng, Qianjian; Yu, Yingmin
PATENT ASSIGNEE(S): Hangzhou Pollen Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 5pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1887858	A	20070103	CN 2006-10052617	20060721

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AB The title method comprises the steps of: (1) condensing trans-4-isopropylcyclohexanecarbonylchloride with D-phenylalanine to obtain crude crystal of B type nateglinide, (2) dissolving the crude crystal in the solution of methanol, aminomethane and water (volume ratio of 60:20:20), heating to 40-60°C, adding 2% active carbon, decoloring for 7-15 min, filtrating, cooling to 10°C to precipitate, filtrating, washing with 40% ethanol till neutral, and drying to obtain H type nateglinide crystal, and (3) recrystg. the mother solution to obtain H type nateglinide crystal. The product of H type nateglinide crystal has good physiol. activity.

L11 ANSWER 2 OF 13 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 145:103952 CASREACT
TITLE: Process for the preparation of nateglinide, preferably in B-form
INVENTOR(S): Vigano, Enrico; Pizzatti, Enrica; Lanfranconi, Simona; Molteni, Renato; Landonio, Ernesto
PATENT ASSIGNEE(S): Italy
SOURCE: U.S. Pat. Appl. Publ., 22 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 2006148902 A1 20060706 US 2005-28283 20050103
PRIORITY APPLN. INFO.: US 2005-28283 20050103
AB The invention relates to a process for the preparation of nateglinide, preferably in B-form, substantially free from the H-form, comprising three steps starting from (i) reaction in an organic solvent between D-phenylalanine Me ester or a salt and trans-4-isopropylcyclohexancarboxylicacid in the presence of an acyl chloride or carbonyldiimidazole, optionally isolating the nateglinide Me ester obtained and re-dissolving it in a second organic solvent, (ii) addition of water and alkali hydroxide to the reaction mixture and separation of the aqueous phase containing the alkali salt of nateglinide, and (iii) addition of hydrochloric acid to the aqueous phase from step (ii) to obtain nateglinide. In an example, the reaction was carried out in acetone in the presence of triethylamine and Et chloroformate and hydrolysis of nateglinide Me ester was carried out using toluene, tricaprylmethylammoniumchloride, and aqueous potassium hydroxide to afford nateglinide in B-form (130.44°C).

L11 ANSWER 3 OF 13 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 144:51894 CASREACT
TITLE: One-pot process for the preparation of nateglinide
INVENTOR(S): Kankan, Rajendra Narayanrao; Rao, Dharmaraj Ramachandra; Singh, Manjinder; Birari, Dilip Ramdas
PATENT ASSIGNEE(S): Cipla Limited, India; Wain, Christopher Paul
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005121071	A1	20051222	WO 2005-GB2267	20050608
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005252002	A1	20051222	AU 2005-252002	20050608
CA 2570041	A1	20051222	CA 2005-2570041	20050608
EP 1765769	A1	20070328	EP 2005-750279	20050608
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
PRIORITY APPLN. INFO.:			GB 2004-13084	20040611
			WO 2005-GB2267	20050608

OTHER SOURCE(S): MARPAT 144:51894
AB A one-pot process for the preparation of nateglinide is presented which comprises amidation of a C1-4 alkyl ester of D-phenylalanine, either as the free base or in salt form (typically the hydrochloride), with

trans-4-isopropylcyclohexanecarboxylicacid or its acid halides to obtain a C1-4 alkyl ester of nateglinide, preferably the Me ester of nateglinide, followed by alkali (e.g., NaOH) saponification and acidification (e.g., HCl) to yield nateglinide (m.p. 128-131°).
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 13 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 143:97635 CASREACT
TITLE: Improved process for the preparation of hypoglycemic agent nateglinide
INVENTOR(S): Zhong, Bohua; Wu, Bo; Yan, Yuan
PATENT ASSIGNEE(S): Toxic Drug Inst., Academy of Military Medical Science, PLA, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, No pp. given
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1517335	A	20040804	CN 2003-100559	20030117
PRIORITY APPLN. INFO.:			CN 2003-100559	20030117

AB A scalable process for the preparation of nateglinide, a hypoglycemic agent, was reported. The key improvement is that the acylation of D-phenylalanine with 4-isopropylcyclohexanecarbonylchloride was performed under a homogeneous condition using a mixture of dioxane or THF and H2O as solvent, largely increasing the yield. Other features include the use of cheap Pd/C instead of previously expensive PtO2 as hydrogenation catalyst in the reduction of 4-isopropylbenzoic acid into 4-isopropylcyclohexanecarboxylicacid. Purification of nateglinide by recrystn. in petroleum ether, hexane and cyclohexane or their mixts. is claimed.

L11 ANSWER 5 OF 13 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 143:26875 CASREACT
TITLE: Improved process for the preparation of hypoglycemic agent nateglinide
INVENTOR(S): Zhu, Qin; Pan, Junfang; Shi, Mingfeng
PATENT ASSIGNEE(S): Shanghai Huashuo Medicine Science & Technology Development Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, No pp. given
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1517334	A	20040804	CN 2003-114970	20030117
PRIORITY APPLN. INFO.:			CN 2003-114970	20030117

AB A scalable process for the preparation of nateglinide, a hypoglycemic agent,

was reported. The key improvement is that the acylation of D-phenylalanine with 4-isopropylcyclohexanecarbonylchloride was performed under a homogeneous condition using a mixture of DMF and H2O as solvent, largely increasing the yield. Other features include the use of cheap Pd/C instead of previously expensive PtO2 as hydrogenation catalyst in the reduction of 4-isopropylbenzoic acid into 4-isopropylcyclohexanecarboxylic acid.

L11 ANSWER 6 OF 13 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 143:7982 CASREACT
TITLE: Process for the preparation of the crystalline B-form nateglinide from D-phenylalanine methyl ester and trans-4-isopropylcyclohexanecarboxylic acid
INVENTOR(S): Vigano', Enrico; Pizzati, Enrica; Lanfranconi, Simona; Molteni, Renato; Landonio, Ernesto
PATENT ASSIGNEE(S): A.M.S.A. Anonima Materie Sintetiche e Affini S.p.A., Italy
SOURCE: Eur. Pat. Appl., 32 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1535900	A1	20050601	EP 2003-27114	20031126
EP 1535900	B1	20061227		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 349418	T	20070115	AT 2003-27114	20031126
PRIORITY APPLN. INFO.:			EP 2003-27114	20031126

AB A process for the preparation of nateglinide comprises: (I) the amidation reaction in a first organic solvent between D-phenylalanine Me ester, or a salt, and trans-4-isopropylcyclohexanecarboxylic acid and an acyl chloride, or carbonyldiimidazole, to obtain the nateglinide Me ester; (Ia) optionally isolating the nateglinide Me ester and redissolving it in a second organic solvent to give a solution; (II) addition of water and alkali hydroxide to the reaction mixture coming from step (I) without isolating the nateglinide Me ester, or, if applicable, to the solution of step (Ia), and separation of the aqueous phase containing the alkali salt of nateglinide; (III) addition of hydrochloric acid to the aqueous phase coming from step (II) to obtain nateglinide, wherein the organic solvent employed in step (II) is a water non-miscible solvent.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 7 OF 13 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 142:317044 CASREACT
TITLE: An efficient large scale synthesis of nateglinide
AUTHOR(S): Chandrasekhar, Batchu; Sawanth, Mangesh S.; Naik, Sameer J.; Gaikwad, Nandakumar B.; Kulkarni, Pramila V.; Bhirud, Shekar B.
CORPORATE SOURCE: Process Research and Development, Glenmark Research Centre, MIDC Mahape, Navi Mumbai, 400709, India

SOURCE: Organic Preparations and Procedures International (2004), 36(5), 459-467
CODEN: OPPIAK; ISSN: 0030-4948
PUBLISHER: Organic Preparations and Procedures, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Nateglinide was prepared as the desired H polymorph by reaction of trans-4-isopropylcyclohexanecarboxylic acid with ClCO2Et and treating the carbonate with D-phenylalanine.
REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 8 OF 13 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 142:156316 CASREACT
TITLE: A saponification and neutralization process for the preparation of chirally pure nateglinide from its lower alkyl esters and nateglinide polymorphic crystalline modifications
INVENTOR(S): Gazdag, Maria; Gizur, Tibor; Hegedus, Bela; Szemzo, Attila; Tarkanyi, Gabor; Toerley, Jozsef; Babjak, Monika
PATENT ASSIGNEE(S): Richter Gedeon Vegyeszeti Gyar Rt., Hung.
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005005373	A1	20050120	WO 2004-HU73	20040708
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
HU 200302174	A2	20050728	HU 2003-2174	20030710
EP 1651591	A1	20060503	EP 2004-743732	20040708
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR				
US 2007043117	A1	20070222	US 2006-564017	20060515
PRIORITY APPLN. INFO.:			HU 2003-2174	20030710
			WO 2004-HU73	20040708

AB The preparation of chirally pure nateglinide by treating a nateglinide lower alkyl ester (e.g., Me ester) with an alkali base (e.g., sodium hydroxide) to yield an alkali salt and neutralizing liberating the salt by addition of an acid (e.g., aqueous HCl) is described as is the preparation of polymorphic crystalline modifications of nateglinide.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 9 OF 13 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 140:199745 CASREACT
TITLE: Synthesis and purification of nateglinide
INVENTOR(S): Naik, Samir Jaivant; Kulkarni, Pramila Vijay; Gaikwad, Nandkumar Baburao; Sawant, Mangesh Shivram; Bhirud, Shekhar; Batchu, Chandrasekhar
PATENT ASSIGNEE(S): Glenmark Pharmaceuticals Limited, India
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004018408	A1	20040304	WO 2003-IB3270	20030812
WO 2004018408	A8	20050310		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IN 2002MU00773	A	20040605	IN 2002-MU773	20020826
AU 2003263386	A1	20040311	AU 2003-263386	20030812
PRIORITY APPLN. INFO.:			IN 2002-MU773	20020826
			WO 2003-IB3270	20030812

OTHER SOURCE(S): MARPAT 140:199745
AB N-[(trans-4-isopropylcyclohexyl)carbonyl]-D-phenylalanin(nateglinide) was prepared by reaction of trans-4-isopropylcyclohexylcarboxylicacid with an alkyl chloroformate in a ketonic solvent in the presence of a base at -20 to 30°C and reaction of the mixed anhydride product with an aqueous alkali salt solution of D-phenylalanine. An example shows the synthesis of nateglinide by using triethylamine and Et chloroformate in acetone (97% pure following HPLC).
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 10 OF 13 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 140:94292 CASREACT
TITLE: Process for preparing nateglinide and its intermediates
INVENTOR(S): Yahalomi, Ronit; Shapiro, Evgeny; Dolitzky, Ben-zion; Gozlan, Yigael
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals Usa, Inc.
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004005240	A1	20040115	WO 2003-US21238	20030703
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003256454	A1	20040123	AU 2003-256454	20030703
EP 1487782	A1	20041222	EP 2003-763310	20030703
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1671649	A	20050921	CN 2003-817439	20030703
US 2004116526	A1	20040617	US 2003-623237	20030718
US 7148376	B2	20061212		
US 2005014949	A1	20050120	US 2003-623290	20030718
US 2005075400	A1	20050407	US 2003-622999	20030718
CN 1723190	A	20060118	CN 2003-821921	20030718
US 2007004804	A1	20070104	US 2006-516363	20060905
PRIORITY APPLN. INFO.:			US 2002-393495P	20020703
			US 2002-396904P	20020718
			US 2002-413622P	20020925
			US 2002-414199P	20020926
			US 2002-423750P	20021105
			US 2002-432093P	20021210
			US 2002-432962P	20021212
			US 2003-442109P	20030123
			US 2003-449791P	20030224
			US 2003-479016P	20030616
			WO 2003-US21238	20030703
			US 2003-622999	20030718

AB A process for the preparation of nateglinide involves converting trans-4-isopropylcyclohexanecarboxylicacid into the acid chloride by reaction with thionyl chloride in the presence of an organic amide and acylation of a suitable salt of D-phenylalaninewith the acid chloride in a single or two phase system or in water free of a co-solvent.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 11 OF 13 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 138:254901 CASREACT
TITLE: a new synthesis method of nateglinide as antidiabetic drug
AUTHOR(S): Wang, Dun; Liang, Yiheng; Gong, Ping; Zhao, Yanfang
CORPORATE SOURCE: School of Pharmaceutical Engineering, Shenyang Pharmaceutical University, Shenyang, 110016, Peop. Rep. China
SOURCE: Zhongguo Yaowu Huaxue Zazhi (2002), 12(2), 94-96
CODEN: ZYHZEF; ISSN: 1005-0108

PUBLISHER: Zhongguo Yaowu Huaxue Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB A new antidiabetic drug-nateglinide was synthesized from isopropylbenzene by Friedel-Crafts reaction, chloroform reaction, catalytic hydrogenation to obtain trans-4-isopropylhexanecarboxylic acid, acylation of D-phenylalanine Et ester, hydrolysis to obtain nateglinide B-type crystal, and crystal-conversion. The total yield was 9.8%.

L11 ANSWER 12 OF 13 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 136:340997 CASREACT
TITLE: Process for preparation of acylphenylalanines
INVENTOR(S): Sumikawa, Michito; Ohgane, Takao
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002032853	A1	20020425	WO 2001-JP9068	20011016
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
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AU 200194264	A	20020429	AU 2001-94264	20011016
CA 2425533	A1	20030410	CA 2001-2425533	20011016
EP 1334962	A1	20030813	EP 2001-974874	20011016
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001014728	A	20031014	BR 2001-14728	20011016
RU 2287520	C2	20061120	RU 2003-111012	20011016
TW 575541	B	20040211	TW 2001-90125695	20011017
IN 2003CN00536	A	20050415	IN 2003-CN536	20030411
US 2004024219	A1	20040205	US 2003-418102	20030418
US 7030268	B2	20060418		
US 2006155143	A1	20060713	US 2005-319177	20051228
PRIORITY APPLN. INFO.:			JP 2000-317603	20001018
			WO 2001-JP9068	20011016
			US 2003-418102	20030418

AB This document discloses a process for preparing easily and simply high-purity acylphenylalanines extremely useful as raw materials of drugs or the like, characterized by reacting an acid chloride with phenylalanine in a mixed solvent consisting of an organic solvent and water under conditions made alkaline with potassium hydroxide.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 13 OF 13 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 136:325825 CASREACT
TITLE: Process for producing nateglinide crystals
INVENTOR(S): Takahashi, Daisuke; Nishi, Seiichi; Takahashi, Satoji
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002032854	A1	20020425	WO 2001-JP9069	20011016
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
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AU 200194265	A	20020429	AU 2001-94265	20011016
CA 2425538	A1	20030410	CA 2001-2425538	20011016
EP 1334963	A1	20030813	EP 2001-974875	20011016
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001014729	A	20031014	BR 2001-14729	20011016
RU 2273629	C2	20060410	RU 2003-111021	20011016
CN 1769263	A	20060510	CN 2005-10118852	20011016
TW 251588	B	20060321	TW 2001-90125697	20011017
IN 2003CN00537	A	20050415	IN 2003-CN537	20030411
US 2004030182	A1	20040212	US 2003-418105	20030418
US 7208622	B2	20070424		
PRIORITY APPLN. INFO.:			JP 2000-317604	20001018
			CN 2001-820658	20011016
			WO 2001-JP9069	20011016

AB A process for producing nateglinide crystals comprises reacting trans-4-isopropylcyclohexylcarbonylchloride with D-phenylalanine in a mixed solvent consisting of a ketone solvent and water in the presence of an alkali to obtain a reaction mixture containing nateglinide, adding an acid to the reaction mixture to make it acidic, and regulating (a) the temperature to 58° to 72° and (b) and the ketone solvent concentration to > 8 weight% and < 22 weight%, to conduct crystallization Nateglinide is a known antidiabetic.
The process is an industrially advantageous method for crystallizing nateglinide.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 17:49:04 ON 02 MAY 2007)

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     FILE 'REGISTRY' ENTERED AT 17:49:18 ON 02 MAY 2007
L1                STRUCTURE UPLOADED
L2             5 S L1 SSS SAM
L3            82 S L1 SSS FULL

     FILE 'HCAPLUS' ENTERED AT 17:50:19 ON 02 MAY 2007
L4            44 S L3/P
L5            14 S SALT? AND L4
                 E US20050234129/PRN,PN,AN
                 E US200500234129/PRN,PN,AN
                 E NATEGLINIDE+ALL/CT
L6             0 S SALT? (W) NATEGLINIDE
L7             1 S "NATEGLINIDE SALT?"
                 E US2005234129/PRN,PN,AN

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     FILE 'REGISTRY' ENTERED AT 18:04:27 ON 02 MAY 2007
L9             9 S  105816-04-4/RN OR 592523-31-4/RN OR 592523-32-5/RN OR 592524

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     FILE 'HCAPLUS' ENTERED AT 18:07:36 ON 02 MAY 2007

     FILE 'STNGUIDE' ENTERED AT 18:08:42 ON 02 MAY 2007

     FILE 'HCAPLUS' ENTERED AT 18:14:39 ON 02 MAY 2007

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L10            0 S  105816-04-4/PRO

     FILE 'CASREACT' ENTERED AT 18:15:57 ON 02 MAY 2007
L11           13 S  105816-04-4/PRO
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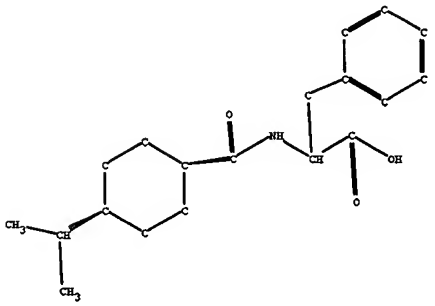

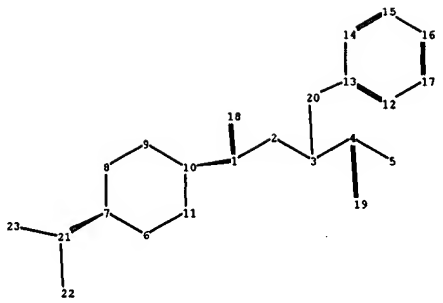

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1 2 3 4 5 18 19 20 21 22 23
ring nodes :
6 7 8 9 10 11 12 13 14 15 16 17
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ring bonds :
6-7 6-11 7-8 8-9 9-10 10-11 12-13 12-17 13-14 14-15 15-16 16-17
exact/norm bonds :
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exact bonds :
1-10 3-4 3-20 7-21 13-20 21-22 21-23
normalized bonds :
4-5 4-19 12-13 12-17 13-14 14-15 15-16 16-17

Match level :
1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:CLASS

Stereo Bonds:

10-1 (Single Wedge).

21-7 (Single Hash).

Stereo Chiral Centers:

7 (Parity=Even)
10 (Parity=Odd)

Stereo RSS Sets:

Type=Relative (Default). 2 Nodes= 7 10

10/507255 SALTS OF NATEGLINIDE -str_regno_text -Search

=> d his

(FILE 'HOME' ENTERED AT 17:49:04 ON 02 MAY 2007)

FILE 'REGISTRY' ENTERED AT 17:49:18 ON 02 MAY 2007
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L2 5 S L1 SSS SAM
L3 82 S L1 SSS FULL

FILE 'HCAPLUS' ENTERED AT 17:50:19 ON 02 MAY 2007
L4 44 S L3/P
L5 14 S SALT? AND L4
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E US200500234129/PRN,PN,AN
E NATEGLINIDE+ALL/CT
L6 0 S SALT? (W) NATEGLINIDE
L7 1 S "NATEGLINIDE SALT?"
E US2005234129/PRN,PN,AN

FILE 'STNGUIDE' ENTERED AT 18:00:24 ON 02 MAY 2007
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FILE 'REGISTRY' ENTERED AT 18:04:27 ON 02 MAY 2007
L9 9 S 105816-04-4/RN OR 592523-31-4/RN OR 592523-32-5/RN OR 592524

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L1      STRUCTURE UPLOADED

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L1              STR
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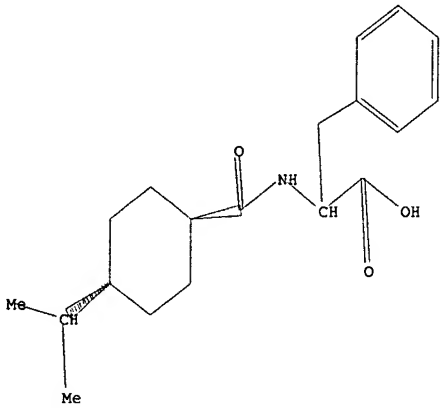


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Structure attributes must be viewed using STN Express query preparation.


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100.0% PROCESSED      441 ITERATIONS                              5 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          7561 TO    10079
PROJECTED ANSWERS:                5 TO      234

L2            5 SEA SSS SAM L1

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SEARCH TIME: 00.00.01

L3           82 SEA SSS FUL L1
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                                                      ENTRY     SESSION
FULL ESTIMATED COST                                  172.55      172.76

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FILE COVERS 1907 - 2 May 2007  VOL 146 ISS 19
FILE LAST UPDATED: 1 May 2007  (20070501/ED)

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 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> s l3/p
L4           44 L3/P

=> s salt? and l4
      1211784 SALT?
L5           14 SALT? AND L4

=> d scan

L5    14 ANSWERS   HCAPLUS  COPYRIGHT 2007 ACS on STN
IC   ICM  C07C231-24
     ICS  C07C233-63; A61K031-16; A61P003-00
CC   63-6 (Pharmaceuticals)
     Section cross-reference(s): 34, 75
TI   Process for the preparation of polymorphic crystalline forms of
     nateglinide ammonium salt
ST   nateglinide ammonium salt polymorphic cryst form
IT   Bicarbonates
     Carbonates, reactions
     RL: RGT (Reagent); RACT (Reactant or reagent)
        (Group IA and IIA metal, bases; process for the preparation of polymorphic
        crystalline forms of nateglinide ammonium salt)
IT   Alkali metal hydroxides
     RL: RGT (Reagent); RACT (Reactant or reagent)
        (base; process for the preparation of polymorphic crystalline forms of
        nateglinide ammonium salt)
IT   Alkali metal hydrides
     Alkaline earth hydroxides
     RL: RGT (Reagent); RACT (Reactant or reagent)
```

(bases; process for the preparation of polymorphic crystalline forms of nateglinide ammonium salt)
IT Crystallization
Neutralization
(in a process for the preparation of polymorphic crystalline forms of nateglinide
ammonium salt)
IT Bases, reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(in a process for the preparation of polymorphic crystalline forms of nateglinide
ammonium salt)
IT Diabetes mellitus
(non-insulin-dependent; process for the preparation of polymorphic crystalline
forms of nateglinide ammonium salt for the treatment of)
IT Polymorphism (crystal)
(process for the preparation of polymorphic crystalline forms of nateglinide ammonium salt)
IT Hyperglycemia
(process for the preparation of polymorphic crystalline forms of nateglinide ammonium salt for the treatment of)
IT Antidiabetic agents
(process for the preparation of polymorphic crystalline forms of nateglinide ammonium salt for use as)
IT Drug delivery systems
(process for the preparation of polymorphic crystalline forms of nateglinide ammonium salt for use in)
IT 1344-28-1D, Alumina, basic
RL: RGT (Reagent); RACT (Reactant or reagent)
(base; process for the preparation of polymorphic crystalline forms of nateglinide ammonium salt)
IT 67-56-1, Methanol, uses 7732-18-5, Water, uses
RL: NUU (Other use, unclassified); USES (Uses)
(process for the preparation of polymorphic crystalline forms of nateglinide ammonium salt)
IT 594837-89-5P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for the preparation of polymorphic crystalline forms of nateglinide ammonium salt)
IT 1336-21-6, Ammonium hydroxide 7664-41-7, Ammonia, reactions
105816-04-4, Nateglinide
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for the preparation of polymorphic crystalline forms of nateglinide ammonium salt)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):3

L5 14 ANSWERS HCAPLUS COPYRIGHT 2007 ACS on STN
IC ICM C07C231-14
ICS C07C233-63
CC 34-2 (Amino Acids, Peptides, and Proteins)
TI Synthesis and purification of nateglinide
ST nateglinide prepn purifn; phenylalanine isopropylcyclohexylcarbonyl prepn purifn
IT 105816-04-4P, Nateglinide
RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)

(synthesis and purification of nateglinide)
IT 79-22-1, Methyl chloroformate 108-23-6, Isopropyl chloroformate 109-61-5, Propyl chloroformate 541-41-3, Ethyl chloroformate 673-06-3, D Phenylalanine 7077-05-6, trans 4 Isopropylcyclohexanecarboxylic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis and purification of nateglinide)

L5 14 ANSWERS HCAPLUS COPYRIGHT 2007 ACS on STN
IC ICM C07C103-84
ICS C07D213-82; C07D307-84; C07C103-737; A61K031-195; A61K031-215
CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
TI Preparation of D-phenylalanine derivatives and their use as hypoglycemic agents
ST hypoglycemic D phenylalanine prepn
IT Antidiabetics and Hypoglycemics
(N-acyl-D-phenylalanines)
IT 6066-82-6, N-Hydroxysuccinimide
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification of, with cyclopentanecarboxylic acid and cumic acid)
IT 536-66-3 3400-45-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification of, with hydroxysuccinimide)
IT 23635-14-5, (S)-(-)-Perillic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(hydrogenation of)
IT 10512-92-2 37002-52-1 74204-45-8 85856-40-2 86808-12-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(hypoglycemic activity of)
IT 7077-05-6P, trans-4-Isopropylcyclohexanecarboxylic acid 7084-93-7P, cis-4-Isopropylcyclohexanecarboxylic acid
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and esterification of)
IT 51871-58-0P 105746-51-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with D-phenylalanine Me ester)
IT 13828-35-8P, Methyl cis-4-isopropylcyclohexanecarboxylate 13828-36-9P, Methyl trans-4-isopropylcyclohexanecarboxylate 105746-50-7P 105746-52-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and saponification of)
IT 62067-45-2P, 4-Isopropylcyclohexanecarboxylic acid
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and N-acylation by, of D-phenylalanine)
IT 75691-91-7P 105746-24-5P 105746-25-6P 105746-26-7P 105746-27-8P 105746-28-9P 105746-29-0P 105746-30-3P 105746-31-4P 105746-32-5P 105746-33-6P 105746-34-7P 105746-35-8P 105746-36-9P 105746-37-0P 105746-38-1P 105746-39-2P 105746-40-5P 105746-41-6P 105746-42-7P 105746-43-8P 105746-44-9P 105746-45-0P 105746-46-1P 105746-47-2P 105746-48-3P 105746-49-4P 105816-04-4P 105816-05-5P 105816-06-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as hypoglycemic)
IT 13033-84-6

RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with carboxylic acid succinimidyl esters)
IT 65-85-0, reactions 98-73-7, 4-tert-Butylbenzoic acid 98-89-5
496-41-3 824-62-4 943-29-3 4771-80-6, 3-Cyclohexenecarboxylic acid
6833-47-2, trans-4-Ethylcyclohexanecarboxylic acid 13064-83-0,
trans-4-Methylcyclohexanecarboxylic acid 16331-45-6, 4-Ethylbenzoyl
chloride 38289-27-9 38289-28-0 65898-38-6, 5-Indanecarboxylic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(N-acylation by, of D-phenylalanine)
IT 673-06-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(N-acylation of)

L5 14 ANSWERS HCAPLUS COPYRIGHT 2007 ACS on STN
IC ICM C07C231-22
ICS C07C231-24; C07C233-63
CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 45, 63, 75
TI Process for the preparation of the crystalline B-form nateglinide from
D-phenylalanine methyl ester and trans-4-isopropylcyclohexanecarboxylic
acid
ST nateglinide prepn polymorphic crystal B form
IT Acid halides
RL: RGT (Reagent); RACT (Reactant or reagent)
(acid chlorides; in a process for the preparation of the crystalline B-form
nateglinide from D-phenylalanine Me ester)
IT Amidation
Neutralization
Saponification
(in a process for the preparation of the crystalline B-form nateglinide from
D-phenylalanine Me ester)
IT Alkali metal hydroxides
RL: RGT (Reagent); RACT (Reactant or reagent)
(in a process for the preparation of the crystalline B-form nateglinide from
D-phenylalanine Me ester)
IT Polymorphism (crystal)
(process for the preparation of the crystalline B-form nateglinide from
D-phenylalanine Me ester)
IT Saponification catalysts
(quaternary ammonium compds.; in a process for the preparation of the
crystalline
B-form nateglinide from D-phenylalanine Me ester)
IT Quaternary ammonium compounds, uses
RL: CAT (Catalyst use); USES (Uses)
(saponification catalysts; in a process for the preparation of the
crystalline B-form
nateglinide from D-phenylalanine Me ester)
IT 5137-55-3, Tricaprylmethylammonium chloride
RL: CAT (Catalyst use); USES (Uses)
(in a process for the preparation of the crystalline B-form nateglinide from
D-phenylalanine Me ester)
IT 673-06-3, D-Phenylalanine 7077-05-6, trans-4-
Isopropylcyclohexanecarboxylic acid 21685-51-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(in a process for the preparation of the crystalline B-form nateglinide from
D-phenylalanine Me ester)
IT 13033-84-6P 105746-47-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(in a process for the preparation of the crystalline B-form nateglinide from
D-phenylalanine Me ester)
IT 530-62-1 541-41-3, Ethyl chloroformate 1310-58-3, Potassium hydroxide,
reactions 1310-65-2, Lithium hydroxide 1310-73-2, Sodium hydroxide,
reactions 3282-30-2, Pivaloyl chloride 7647-01-0, Hydrogen chloride,
reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(in a process for the preparation of the crystalline B-form nateglinide from
D-phenylalanine Me ester)
IT 105816-04-4P, Nateglinide
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(process for the preparation of the crystalline B-form nateglinide from
D-phenylalanine Me ester)
IT 67-64-1, Acetone, uses 68-12-2, DMF, uses 71-43-2, Benzene, uses
75-09-2, Dichloromethane, uses 108-88-3, Toluene, uses 108-90-7,
Chlorobenzene, uses 109-99-9, Thf, uses 110-54-3, Hexane, uses
110-71-4, Glyme 110-82-7, Cyclohexane, uses 111-96-6, Diglyme
123-91-1, Dioxane, uses 127-19-5, Dimethylacetamide 142-82-5, Heptane,
uses 872-50-4, NMP, uses 1330-20-7, Xylene, uses 7732-18-5, Water,
uses
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; in a process for the preparation of the crystalline B-form
nateglinide
from D-phenylalanine Me ester)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

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(FILE 'HOME' ENTERED AT 17:49:04 ON 02 MAY 2007)

FILE 'REGISTRY' ENTERED AT 17:49:18 ON 02 MAY 2007
L1 STRUCTURE UPLOADED
L2 5 S L1 SSS SAM
L3 82 S L1 SSS FULL

FILE 'HCAPLUS' ENTERED AT 17:50:19 ON 02 MAY 2007
L4 44 S L3/P
L5 14 S SALT? AND L4

=> d 15 1-14 ibib abs

L5 ANSWER 1 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:657506 HCAPLUS
DOCUMENT NUMBER: 145:103952
TITLE: Process for the preparation of nateglinide, preferably
in B-form
INVENTOR(S): Vigano, Enrico; Pizzatti, Enrica; Lanfranconi, Simona;
Molteni, Renato; Landonio, Ernesto
PATENT ASSIGNEE(S): Italy
SOURCE: U.S. Pat. Appl. Publ., 22 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 2006148902 A1 20060706 US 2005-28283 20050103
PRIORITY APPLN. INFO.: US 2005-28283 20050103
OTHER SOURCE(S): CASREACT 145:103952
AB The invention relates to a process for the preparation of nateglinide, preferably in B-form, substantially free from the H-form, comprising three steps starting from (i) reaction in an organic solvent between D-phenylalanine Me ester or a salt and trans-4-isopropylcyclohexancarboxylic acid in the presence of an acyl chloride or carbonyldiimidazole, optionally isolating the nateglinide Me ester obtained and re-dissolving it in a second organic solvent, (ii) addition of water and alkali hydroxide to the reaction mixture and separation of the aqueous phase containing the alkali salt of nateglinide, and (iii) addition of hydrochloric acid to the aqueous phase from step (ii) to obtain nateglinide. In an example, the reaction was carried out in acetone in the presence of triethylamine and Et chloroformate and hydrolysis of nateglinide Me ester was carried out using toluene, tricaprylmethylammonium chloride, and aqueous potassium hydroxide to afford nateglinide in B-form (130.44°C).

L5 ANSWER 2 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1328488 HCAPLUS
DOCUMENT NUMBER: 144:51894
TITLE: One-pot process for the preparation of nateglinide
INVENTOR(S): Kankan, Rajendra Narayanrao; Rao, Dharmaraj Ramachandra; Singh, Manjinder; Birari, Dilip Ramdas
PATENT ASSIGNEE(S): Cipla Limited, India; Wain, Christopher Paul
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005121071	A1	20051222	WO 2005-GB2267	20050608
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005252002	A1	20051222	AU 2005-252002	20050608
CA 2570041	A1	20051222	CA 2005-2570041	20050608
EP 1765769	A1	20070328	EP 2005-750279	20050608
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				

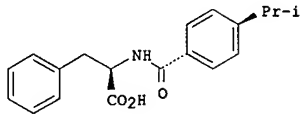
PRIORITY APPLN. INFO.: GB 2004-13084 A 20040611
WO 2005-GB2267 W 20050608
OTHER SOURCE(S): CASREACT 144:51894; MARPAT 144:51894
AB A one-pot process for the preparation of nateglinide is presented which comprises amidation of a C1-4 alkyl ester of D-phenylalanine, either as the free base or in salt form (typically the hydrochloride),

with trans-4-isopropylcyclohexanecarboxylic acid or its acid halides to obtain a C1-4 alkyl ester of nateglinide, preferably the Me ester of nateglinide, followed by alkali (e.g., NaOH) saponification and acidification (e.g., HCl) to yield nateglinide (m.p. 128-131°).
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1261034 HCAPLUS
DOCUMENT NUMBER: 144:23128
TITLE: Stable nateglinide form b compositions via crystallization
INVENTOR(S): Venkataraman, Sundaram; Narsapur, Sharat Pandurang; Kharkar, Manoj Ramesh; Bangarubabu, Rongali; Sandeep, Mohanty; Sayantani, Pyne; Raju, Kakarlapudi Ranga
PATENT ASSIGNEE(S): Dr. Reddy's Laboratories Ltd., India; Dr. Reddy's Laboratories, Inc.
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005113485	A2	20051201	WO 2005-US17664	20050520
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2004-572689P P 20040520
US 2004-586431P P 20040708
US 2005-644614P P 20050118
GI



I

AB A process for preparing nateglinide Form B comprises dissolving nateglinide (I) in a solvent and adding the solution, at temps. of 40-45°C, to a hydrocarbon liquid that is at temps. of 40-45°C. Then, water is added and the mixture is allowed to cool, producing crystals of nateglinide

Form B.

L5 ANSWER 4 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1240947 HCAPLUS
DOCUMENT NUMBER: 144:11582
TITLE: Process for the preparation of polymorphic crystalline forms of nateglinide ammonium salt
INVENTOR(S): Wizel, Shlomit; Frenkel, Gustavo; Gome, Boaz
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals Usa, Inc.
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005110972	A1	20051124	WO 2005-US16343	20050509
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2563793	A1	20051124	CA 2005-2563793	20050509
US 2006004102	A1	20060105	US 2005-126050	20050509
EP 1656339	A1	20060517	EP 2005-748381	20050509
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU				
CN 1950331	A	20070418	CN 2005-80014509	20050509
PRIORITY APPLN. INFO.:			US 2004-569047P P	20040507
			WO 2005-US16343 W	20050509

AB Anti-hyperglycemic polymorphic crystalline forms of nateglinide ammonium salt are prepared
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:467801 HCAPLUS
DOCUMENT NUMBER: 143:7982
TITLE: Process for the preparation of the crystalline B-form nateglinide from D-phenylalanine methyl ester and trans-4-isopropylcyclohexanecarboxylic acid
INVENTOR(S): Vigano', Enrico; Pizzati, Enrica; Lanfranconi, Simona; Molteni, Renato; Landonio, Ernesto
PATENT ASSIGNEE(S): A.M.S.A. Anonima Materie Sintetiche e Affini S.p.A., Italy
SOURCE: Eur. Pat. Appl., 32 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

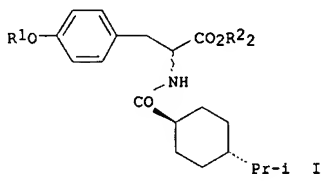
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1535900	A1	20050601	EP 2003-27114	20031126
EP 1535900	B1	20061227		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 349418	T	20070115	AT 2003-27114	20031126
PRIORITY APPLN. INFO.:			EP 2003-27114 A	20031126

OTHER SOURCE(S): CASREACT 143:7982
AB A process for the preparation of nateglinide comprises: (I) the amidation reaction in a first organic solvent between D-phenylalanine Me ester, or a salt, and trans-4-isopropylcyclohexanecarboxylic acid and an acyl chloride, or carbonyldiimidazole, to obtain the nateglinide Me ester; (Ia) optionally isolating the nateglinide Me ester and redissolving it in a second organic solvent to give a solution; (II) addition of water and alkali hydroxide to the reaction mixture coming from step (I) without isolating the nateglinide Me ester, or, if applicable, to the solution of step (Ia), and separation of the aqueous phase containing the alkali salt of nateglinide; (III) addition of hydrochloric acid to the aqueous phase coming from step (II) to obtain nateglinide , wherein the organic solvent employed in step (II) is a water non-miscible solvent.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:414565 HCAPLUS
DOCUMENT NUMBER: 142:482315
TITLE: Preparation of alanine derivative as antidiabetics
INVENTOR(S): Yang, Yushe; Tang, Lei; Ji, Ruyun; Chen, Kaixian
PATENT ASSIGNEE(S): Shanghai Institute of Pharmacy, Chinese Academy of Sciences, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 26 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1431197	A	20030723	CN 2003-115160	20030124
PRIORITY APPLN. INFO.:			CN 2003-115160	20030124

OTHER SOURCE(S): CASREACT 142:482315; MARPAT 142:482315
GI



AB Alanine derivs. I (R1 = 2-(1-indolyl)ethyl, 2-[N-(2-benzoxazolyl)-N-methyl]aminoethyl, 2-[N-methyl-N-(2-pyridinyl)]aminoethyl, 2-(4-methyl-2-phenyl-4-oxazolyl)ethyl, 4-trifluoromethylbenzyl, benzyl; R2 = H, alkyl) is prepared by condensation reaction of trans-4-isopropylcyclohexanecarboxylic acid N-succinimidyl ester with L- or D-tyrosine Me ester in inert solvent to obtain 3-(4-hydroxyphenyl)-2-(trans-isopropylcyclohexylcarboxamido)propanoic acid Me ester (II), Mitsunobu reaction with aromatic alc., and then hydrolysis with inorg. base solution The method may be prepared by (1) etherification of II with alkyl halide in alkaline medium; (2) hydrolysis of II; or (3) condensation reaction of II with amino-protected 2-methylaminoethanol, condensation reaction with 2-fluoropyridine, and hydrolysis with base. The alanine derivative and its salt may be used to prepare the medical prepns. for treating type II diabetes mellitus.

L5 ANSWER 7 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:59980 HCAPLUS
DOCUMENT NUMBER: 142:141289
TITLE: Crystalline form of nateglinide
INVENTOR(S): Frenkel, Gustavo; Gome, Boaz; Wizel, Shlomit
PATENT ASSIGNEE(S): Israel
SOURCE: U.S. Pat. Appl. Publ., 91 pp., Cont.-in-part of U.S. Ser. No. 622,905.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005014836	A1	20050120	US 2003-746697	20031224
US 2004181089	A1	20040916	US 2003-622905	20030718
CA 2513753	A1	20040812	CA 2004-2513753	20040113
WO 2004067496	A1	20040812	WO 2004-US839	20040113
WO 2004067496	A9	20041209		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
EP 1511717	A1	20050309	EP 2004-701826	20040113
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1835912	A	20060920	CN 2004-80005672	20040113
US 2007004804	A1	20070104	US 2006-516363	20060905
PRIORITY APPLN. INFO.:			US 2003-442109P	P 20030123

US 2003-449791P	P	20030224
US 2003-479016P	P	20030616
US 2003-622905	A2	20030718
US 2002-396904P	P	20020718
US 2002-413622P	P	20020925
US 2002-414199P	P	20020926
US 2002-423750P	P	20021105
US 2002-432093P	P	20021210
US 2002-432962P	P	20021212
US 2003-622999	A1	20030718
WO 2003-US22375	A	20030718
US 2003-693166	A	20031023
US 2003-746697	A	20031224
WO 2004-US839	W	20040113

AB Crystalline forms of nateglinide and processes for their preparation, as well as pharmaceutical formulations containing them and methods of administration are provided. A process for preparing crystalline form of nateglinide comprises the steps of(a) preparing a solution of nateglinide in Et acetate, (b) seeding the solution with nateglinide crystals, and (c) recovering the crystalline form as a precipitate The nateglinide obtained is more than about 99% pure. For example, nateglinide (5 g) was dissolved in acetonitrile, acetone, or Et acetate at about 55° in over about 15 min until a clear solution was obtained. The solvent was removed to dryness by evaporation at about 55°/20 to 30 mmHg to give dry nateglinide crystalline Form B. Also, nateglinide Form Z was prepared by treating 7.73 g of D-phenylalanine (PheOH) with 185 mL (3.5 equiv) of 3.5% NaOH at room temperature to afford a clear solution of the corresponding Na-salt. A solution of neat trans-4-isopropylcyclohexanecarboxyl chloride (IPCHAC, 9.02 g, 1.01 equiv) was added to the solution of Phe-OH obtained above, over 3 min, while stirring at room temperature The rest of the IPCHAC in the funnel was washed with toluene (1 mL) and added. The resulting mixture was stirred for 1 h, and was treated with 10% HCl (32 mL) to adjust the pH to 3, while stirring. The mixture was stirred for 1 h, and filtered. The solid was washed with water (200 mL) and sucked well to afford 33.3 g of the moist product, which lost weight after drying at 78°/2.2 mbar (Assay 98.4%, purity >99% , yield 86%).

L5 ANSWER 8 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:55192 HCAPLUS
DOCUMENT NUMBER: 142:156316
TITLE: A saponification and neutralization process for the preparation of chirally pure nateglinide from its lower alkyl esters and nateglinide polymorphic crystalline modifications
INVENTOR(S): Gazdag, Maria; Gizur, Tibor; Hegedus, Bela; Szemzo, Attila; Tarkanyi, Gabor; Toerley, Jozsef; Babjak, Monika
PATENT ASSIGNEE(S): Richter Gedeon Vegyeszeti Gyar Rt., Hung.
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2005005373	A1	20050120	WO 2004-HU73		20040708
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
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HU 200302174	A2	20050728	HU 2003-2174		20030710
EP 1651591	A1	20060503	EP 2004-743732		20040708
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US 2007043117	A1	20070222	US 2006-564017		20060515
PRIORITY APPLN. INFO.:			HU 2003-2174	A	20030710
			WO 2004-HU73	W	20040708

OTHER SOURCE(S): CASREACT 142:156316

AB The preparation of chirally pure nateglinide by treating a nateglinide lower alkyl ester (e.g., Me ester) with an alkali base (e.g., sodium hydroxide) to yield an alkali salt and neutralizing liberating the salt by addition of an acid (e.g., aqueous HCl) is described as is the preparation of polymorphic crystalline modifications of nateglinide.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:182826 HCAPLUS
DOCUMENT NUMBER: 140:199745
TITLE: Synthesis and purification of nateglinide
INVENTOR(S): Naik, Samir Jaivant; Kulkarni, Pramila Vijay; Gaikwad, Nandkumar Baburao; Sawant, Mangesh Shivram; Bhirud, Shekhar; Batchu, Chandrasekhar
PATENT ASSIGNEE(S): Glenmark Pharmaceuticals Limited, India
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004018408	A1	20040304	WO 2003-IB3270		20030812
WO 2004018408	A8	20050310			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					

IN 2002MU00773	A	20040605	IN 2002-MU773		20020826
AU 2003263386	A1	20040311	AU 2003-263386		20030812
PRIORITY APPLN. INFO.:			IN 2002-MU773	A	20020826
			WO 2003-IB3270	W	20030812

OTHER SOURCE(S): CASREACT 140:199745; MARPAT 140:199745

AB N-[(trans-4-isopropylcyclohexyl)carbonyl]-D-phenylalanine (nateglinide) was prepared by reaction of trans-4-isopropylcyclohexylcarboxylic acid with an alkyl chloroformate in a ketonic solvent in the presence of a base at -20 to 30°C and reaction of the mixed anhydride product with an aqueous alkali salt solution of D-phenylalanine. An example shows the synthesis of nateglinide by using triethylamine and Et chloroformate in acetone (97% pure following HPLC).

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 10 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:41431 HCAPLUS
DOCUMENT NUMBER: 140:94292
TITLE: Process for preparing nateglinide and its intermediates
INVENTOR(S): Yahalomi, Ronit; Shapiro, Evgeny; Dolitzky, Ben-zion; Gozlan, Yigael
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals Usa, Inc.
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004005240	A1	20040115	WO 2003-US21238		20030703
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AU 2003256454	A1	20040123	AU 2003-256454		20030703
EP 1487782	A1	20041222	EP 2003-763310		20030703
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CN 1671649	A	20050921	CN 2003-817439		20030703
US 2004116526	A1	20040617	US 2003-623237		20030718
US 7148376	B2	20061212			
US 2005014949	A1	20050120	US 2003-623290		20030718
US 2005075400	A1	20050407	US 2003-622999		20030718
CN 1723190	A	20060118	CN 2003-821921		20030718
US 2007004804	A1	20070104	US 2006-516363		20060905
PRIORITY APPLN. INFO.:			US 2002-393495P	P	20020703
			US 2002-396904P	P	20020718
			US 2002-413622P	P	20020925
			US 2002-414199P	P	20020926

US 2002-423750P	P	20021105
US 2002-432093P	P	20021210
US 2002-432962P	P	20021212
US 2003-442109P	P	20030123
US 2003-449791P	P	20030224
US 2003-479016P	P	20030616
WO 2003-US21238	W	20030703
US 2003-622999	A1	20030718

OTHER SOURCE(S): CASREACT 140:94292

AB A process for the preparation of nateglinide involves converting trans-4-isopropylcyclohexanecarboxylic acid into the acid chloride by reaction with thionyl chloride in the presence of an organic amide and acylation of a suitable salt of D-phenylalanine with the acid chloride in a single or two phase system or in water free of a co-solvent.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:737716 HCAPLUS
DOCUMENT NUMBER: 139:230996
TITLE: Preparation and properties of nateglinide salts
INVENTOR(S): Sutton, Paul Allen; Vivilecchia, Richard Victor; Parker, David John; De La Cruz, Marilyn
PATENT ASSIGNEE(S): Novartis Ag, Switz.; Novartis Pharma Gmbh
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003076393	A1	20030918	WO 2003-EP2447	20030310
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
CA 2478599	A1	20030918	CA 2003-2478599	20030310
AU 2003214112	A1	20030922	AU 2003-214112	20030310
EP 1483232	A1	20041208	EP 2003-709769	20030310
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BR 2003008316	A	20041228	BR 2003-8316	20030310
JP 2005519949	T	20050707	JP 2003-574615	20030310
CN 1642904	A	20050720	CN 2003-805803	20030310
US 2005234129	A1	20051020	US 2004-507255	20040928

PRIORITY APPLN. INFO.:	US 2002-363178P	P	20020311
	WO 2003-EP2447	W	20030310

AB The invention relates to salts of nateglinide having specified properties (m.ps., solubilities, X-ray diffraction patterns) for use in pharmaceutical compns. for preventing or treating diabetes, cardiovascular diseases, etc. Nateglinide Na, K, Ca, Mg, N-methyl-D-glucamine, TRIS, lysine, and ammonium salts were prepared and their properties

tabulated.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 12 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:293592 HCAPLUS
DOCUMENT NUMBER: 136:325420
TITLE: Drugs for diabetes, especially type 2, comprising an antiinflammatory or analgesic drug, selected bivalent linkers, and a nitrate ester
INVENTOR(S): Del Soldato, Piero
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002030867	A2	20020418	WO 2001-EP11665	20011009
WO 2002030867	A3	20020725		
W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IT 2000MI2201	A1	20020412	IT 2000-MI2201	20001012
IT 1319201	B1	20030926		
CA 2425655	A1	20020418	CA 2001-2425655	20011009
AU 200214006	A	20020422	AU 2002-14006	20011009
EP 1324974	A2	20030709	EP 2001-982414	20011009
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004511456	T	20040415	JP 2002-534256	20011009
US 2004023890	A1	20040205	US 2003-398511	20030411

PRIORITY APPLN. INFO.:	IT 2000-MI2201	A	20001012
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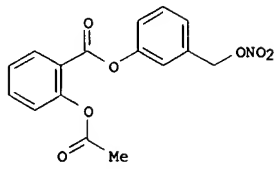
OTHER SOURCE(S): MARPAT 136:325420
GI



II

AB Useful for the treatment of diabetes, particularly type 2, are compds. or salts thereof, having the following general formula

A-(B)n-(C)m-NO2 [I; wherein A = radical of a drug having an antiinflammatory or analgesic activity; B = bivalent linking group wherein the precursor must meet certain tests described in the application; C = another defined bivalent linking group; n and m = 0 or 1, provided that (n + m) = 1 or 2]. I can be used in conjunction with other antidiabetic drugs, particularly insulin. I increase the direct antidiabetic effect of insulin, and reduce complications of diabetes, particularly vascular diseases, retinopathies, neuropathies, etc.. The values of n and m, i.e., the presence or absence of bivalent linkers B and C, alone or in combination, are based on performance of the precursors of the linkers in certain tests (no data). These tests are designated as follows: (test 4A): inhibition by > 15% of hemolysis of rat erythrocytes induced by cumene hydroperoxide; (test 5): inhibition of radical production by ≥ 50% in the oxidative degradation of . desoxyribose in aqueous Fe2+(NH4)2(SO4)2/thiobarbituric acid solution; and (test 4): inhibition by ≥ 50% of DPPH-induced radical production in MeOH solution For instance, acetylsalicylic acid chloride was esterified with 3-(hydroxymethyl)phenol (80%), followed by nitation of the resultant Ph ester with HNO3/H2SO4 (82%), to give invention compound II, which is thus the 3-(nitrooxymethyl)phenyl ester of aspirin. When tested on isolated aorta from insulin-resistant rats, compound II at a concentration of 10-4 M gave 70% vasorelaxation, relative to non-insulin-resistant controls. This effect was unchanged by the presence or absence of the irreversible NO synthetase inhibitor LNNA. In contrast, both Na nitroprussiate and the indomethacin analog of II, known NO donors, were inactive, and the antidiabetic drug metformin was inactivated by LNNA.

L5 ANSWER 13 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1987:85057 HCAPLUS
Correction of: 1987:19047
DOCUMENT NUMBER: 106:85057
Correction of: 106:19047
TITLE: Preparation of D-phenylalanine derivatives and their use as hypoglycemic agents
INVENTOR(S): Toyoshima, Shigeshi; Seto, Yoshiko; Shinkai, Hisashi; Toi, Koji; Kumashiro, Izumi
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: Eur. Pat. Appl., 25 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 196222	A2	19861001	EP 1986-302217	19860326
EP 196222	A3	19880224		
EP 196222	B1	19920129		
R: CH, DE, FR, GB, LI				
JP 63054321	A	19880308	JP 1986-61833	19860319
JP 04015221	B	19920317		
US 4816484	A	19890328	US 1988-146719	19880121
US 34878	E	19950314	US 1993-157564	19931123

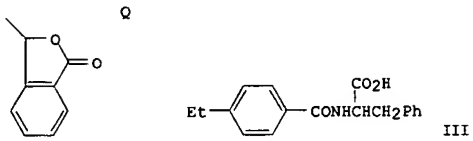
PRIORITY APPLN. INFO.: JP 1985-62276 A 19850327
JP 1986-38111 A1 19860222
US 1986-844970 A3 19860327
US 1988-146719 A5 19880121
US 1989-844970 B3 19890327

OTHER SOURCE(S): CASREACT 106:85057; MARPAT 106:85057
AB D-Phenylalanine derivs. D-R2CONR3CH(CO2R1)CH2Ph [I; R1 = H, C1-5 alkyl, C6-12 aryl or aralkyl, Q, CH2CO2R3, CHMeOCOR3, CH2OCOCMe3; R2 = (un)substituted C6-12 aryl, 5- or 6-membered heterocyclyl, cycloalkyl, cycloalkenyl; R3 = H, C1-5 alkyl], their salts. and precursors which can be converted thereto in the human or animal body, useful as hypoglycemics, were prepared via conventional N-acylating reactions. D-Phenylalanine in 10% aqueous NaOH was successively treated with Me2CO, 4-EtC6H4COCl in Me2CO, and 10% aqueous NaOH to give 83% acylphenylanine D-II. At 25 mg/kg in mice, D-II decreased blood glucose 34% in min.

L5 ANSWER 14 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1987:19047 HCAPLUS
DOCUMENT NUMBER: 106:19047
TITLE: Preparation of D-phenylalanine derivatives and their use as hypoglycemic agents
INVENTOR(S): Toyoshima, Shigeshi; Seto, Yoshiko; Shinkai, Hisashi; Toi, Koji; Kumashiro, Izumi
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: Eur. Pat. Appl., 25 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 196222 A2		19861001	EP 1986-302217	19860326
R: CH, DE, FR, GB, LI				

PRIORITY APPLN. INFO.: JP 1985-62276 19850327
GI



III

AB D-Phenylalanine derivs. D-R2CONR3CH(CO2R1)CH2Ph [I; R1 = H, C1-5 alkyl, C6-12 aryl or aralkyl, Q, CH2CO2R3, CHMeOCOR3, CH2OCOCMe3; R2 = (un)substituted C6-12 aryl, 5- or 6-membered heterocyclyl, cycloalkyl, cycloalkenyl; R3 = H, C1-5 alkyl], their salts, and precursors which can be converted thereto in the human or animal body, useful as hypoglycemics, were prepared via conventional N-acylating reactions. D-Phenylalanine in 10% aqueous NaOH was successively treated with Me2CO, 4-EtC6H4COCl in Me2CO, and 10% aqueous NaOH to give 83% acylphenylanine D-II. At 25 mg/kg in mice, D-II decreased blood glucose 34% in 60 min.

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                E US200500234129/PRN,PN,AN

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        620279 "SALTS"
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L7   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2003:737716  HCAPLUS
DOCUMENT NUMBER:          139:230996
TITLE:                    Preparation and properties of nateglinide
                          salts
INVENTOR(S):              Sutton, Paul Allen; Vivilecchia, Richard Victor;
                          Parker, David John; De La Cruz, Marilyn
PATENT ASSIGNEE(S):       Novartis Ag, Switz.; Novartis Pharma Gmbh
SOURCE:                   PCT Int. Appl., 46 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

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     WO 2003076393         A1    20030918    WO 2003-EP2447           20030310
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     EP 1483232            A1    20041208    EP 2003-709769           20030310
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     JP 2005519949         T     20050707    JP 2003-574615           20030310
     CN 1642904            A     20050720    CN 2003-805803           20030310
     US 2005234129         A1    20051020    US 2004-507255           20040928
PRIORITY APPLN. INFO.:                       US 2002-363178P      P   20020311
                                             WO 2003-EP2447       W   20030310
AB   The invention relates to salts of nateglinide having specified properties
     (m.ps., solubilities, X-ray diffraction patterns) for use in
     pharmaceutical compns. for preventing or treating diabetes, cardiovascular
     diseases, etc.  Nateglinide Na, K, Ca, Mg, N-methyl-D-glucamine, TRIS,
     lysine, and ammonium salts were prepared and their properties tabulated.
REFERENCE COUNT:          3     THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


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E7            2     US2005234131/PN
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E9            1     US2005234133/PN
E10           1     US2005234134/PN
E11           1     US2005234135/PN
E12           1     US2005234136/PN

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     (FILE 'HOME' ENTERED AT 17:49:04 ON 02 MAY 2007)

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L2             5 S L1 SSS SAM
L3            82 S L1 SSS FULL

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L4            44 S L3/P
L5            14 S SALT? AND L4
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                E US200500234129/PRN,PN,AN
                E NATEGLINIDE+ALL/CT
L6             0 S SALT? (W) NATEGLINIDE
L7             1 S "NATEGLINIDE SALT?"
                E US2005234129/PRN,PN,AN

=> d l7 ibib it

L7   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2003:737716  HCAPLUS
DOCUMENT NUMBER:          139:230996
TITLE:                    Preparation and properties of nateglinide
                          salts
INVENTOR(S):              Sutton, Paul Allen; Vivilecchia, Richard Victor;
                          Parker, David John; De La Cruz, Marilyn
PATENT ASSIGNEE(S):       Novartis Ag, Switz.; Novartis Pharma Gmbh
SOURCE:                   PCT Int. Appl., 46 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    -------------------    --------
     WO 2003076393        A1    20030918    WO 2003-EP2447         20030310
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU,
             LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC,
             SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW
         RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE,
             DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,
             SI, SK, TR
     CA 2478599           A1    20030918    CA 2003-2478599        20030310
     AU 2003214112        A1    20030922    AU 2003-214112         20030310
     EP 1483232           A1    20041208    EP 2003-709769         20030310
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
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     BR 2003008316        A     20041228    BR 2003-8316           20030310
     JP 2005519949        T     20050707    JP 2003-574615         20030310
     CN 1642904           A     20050720    CN 2003-805803         20030310
     US 2005234129        A1    20051020    US 2004-507255         20040928
PRIORITY APPLN. INFO.:                      US 2002-363178P     P  20020311
                                            WO 2003-EP2447      W  20030310

IT   Heart, disease
       (angina pectoris; preparation and properties of nateglinide
       salts)
IT   Artery, disease
       (coronary; preparation and properties of nateglinide salts
       )
IT   Kidney, disease
       (diabetic nephropathy; preparation and properties of nateglinide
       salts)
IT   Nerve, disease
       (diabetic neuropathy; preparation and properties of nateglinide
       salts)
IT   Eye, disease
       (diabetic retinopathy; preparation and properties of nateglinide
       salts)
IT   Ulcer
       (foot; preparation and properties of nateglinide salts)
IT   Kidney, disease
       (glomerulosclerosis; preparation and properties of nateglinide
       salts)
IT   Sexual disorders
       (impotence; preparation and properties of nateglinide
       salts)
IT   Heart, disease
       (infarction; preparation and properties of nateglinide
       salts)
IT   Eye, disease
       (macula, degeneration; preparation and properties of nateglinide
       salts)
IT   Acidosis
       (metabolic; preparation and properties of nateglinide
       salts)
IT   Ovary, disease
       (polycystic; preparation and properties of nateglinide
       salts)
IT   Ovarian cycle
       (premenstrual syndrome; preparation and properties of nateglinide
       salts)
IT   Antiarthritics
     Antidiabetic agents
     Antihypertensives
     Antiobesity agents
     Arthritis
     Cardiovascular system, disease
     Cataract
     Connective tissue, disease
     Diabetes insipidus
     Hyperglycemia
     Hypertension
     Obesity
     Osteoporosis
     Skin, disease
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X-ray diffraction
(preparation and properties of nateglinide salts)
IT Hyperlipidemia
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation and properties of nateglinide salts)
IT Artery, disease
(restenosis; preparation and properties of nateglinide salts)
IT Brain, disease
(stroke; preparation and properties of nateglinide salts)
IT Inflammation
Intestine, disease
(ulcerative colitis; preparation and properties of nateglinide salts)
IT 50-99-7, D-Glucose, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(impaired tolerance; preparation and properties of nateglinide salts)
IT 105816-04-4, Nateglinide
RL: PRP (Properties); RCT (Reactant); RACT (Reactant or reagent)
(preparation and properties of nateglinide salts)
IT 592523-31-4P 592523-32-5P 592524-24-8P 594837-85-1P 594837-86-2P
594837-87-3P 594837-88-4P 594837-89-5P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and properties of nateglinide salts)
IT 9004-10-8, Insulin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(resistance; preparation and properties of nateglinide salts)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> fil stng
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 88.17 260.93

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE ENTRY TOTAL SESSION
CA SUBSCRIBER PRICE -11.70 -11.70

FILE 'STNGUIDE' ENTERED AT 18:00:24 ON 02 MAY 2007
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY, JAPAN SCIENCE
AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Apr 27, 2007 (20070427/UP).

=> s 105816-04-4/rn or 592523-31-4/rn or 592523-32-5/rn or 592524-24-8/rn or 594837-85-1/rn or 594837-86-2/rn or 594837-87-3/rn or 594837-88-4/rn or 594837-89-5/rn
'RN' IS NOT A VALID FIELD CODE
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0 594837-86-2/RN
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FULL ESTIMATED COST 0.42 261.35

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE ENTRY TOTAL SESSION
CA SUBSCRIBER PRICE 0.00 -11.70

FILE 'REGISTRY' ENTERED AT 18:04:27 ON 02 MAY 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 1 MAY 2007 HIGHEST RN 934050-43-8
DICTIONARY FILE UPDATES: 1 MAY 2007 HIGHEST RN 934050-43-8

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

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1 594837-86-2/RN
1 594837-87-3/RN
1 594837-88-4/RN
1 594837-89-5/RN
L9 9 105816-04-4/RN OR 592523-31-4/RN OR 592523-32-5/RN OR 592524-24-8/RN OR 594837-85-1/RN OR 594837-86-2/RN OR 594837-87-3/RN OR 594837-88-4/RN OR 594837-89-5/RN

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=> d 19 hitstr
'HITSTR' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'

The following are valid formats:

Substance information can be displayed by requesting individual
fields or predefined formats.  The predefined substance formats
are:  (RN = CAS Registry Number)

REG    - RN
SAM    - Index Name, MF, and structure - no RN
FIDE   - All substance data, except sequence data
IDE    - FIDE, but only 50 names
SQIDE  - IDE, plus sequence data
SQIDE3 - Same as SQIDE, but 3-letter amino acid codes are used
SQD    - Protein sequence data, includes RN
SQD3   - Same as SQD, but 3-letter amino acid codes are used
SQN    - Protein sequence name information, includes RN

CALC   - Table of calculated properties
EPROP  - Table of experimental properties
PROP   - EPROP and CALC

Any CA File format may be combined with any substance format to
obtain CA references citing the substance.  The substance formats
must be cited first.  The CA File predefined formats are:

ABS  -- Abstract
APPS -- Application and Priority Information,
BIB  -- CA Accession Number, plus Bibliographic Data
CAN  -- CA Accession Number
CBIB -- CA Accession Number, plus Bibliographic Data (compressed)
IND  -- Index Data
IPC  -- International Patent Classification
PATS -- PI, SO
STD  -- BIB, IPC, and NCL

IABS -- ABS, indented, with text labels
IBIB -- BIB, indented, with text labels
ISTD -- STD format, indented

OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

The ALL format gives FIDE BIB ABS IND RE, plus sequence data when
it is available.
The MAX format is the same as ALL.
The IALL format is the same as ALL with BIB ABS and IND indented,
with text labels.

For additional information, please consult the following help
messages:

HELP DFIELDS -- To see a complete list of individual display fields.
HELP FORMATS -- To see detailed descriptions of the predefined formats.
ENTER DISPLAY FORMAT (IDE):ide
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L9   ANSWER 1 OF 9  REGISTRY  COPYRIGHT 2007 ACS on STN
RN   594837-89-5  REGISTRY
ED   Entered STN:  29 Sep 2003
CN   D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-,
     ammonium salt (9CI)  (CA INDEX NAME)
FS   STEREOSEARCH
MF   C19 H27 N O3 . x H3 N
SR   CA
LC   STN Files:   CA, CAPLUS, USPATFULL
CRN  (105816-04-4)

Absolute stereochemistry.
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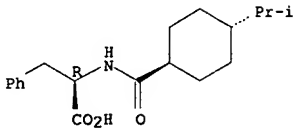

●x NH_3

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               2 REFERENCES IN FILE CAPLUS (1907 TO DATE)


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     (FILE 'HOME' ENTERED AT 17:49:04 ON 02 MAY 2007)

     FILE 'REGISTRY' ENTERED AT 17:49:18 ON 02 MAY 2007
L1              STRUCTURE UPLOADED
L2            5 S L1 SSS SAM
L3           82 S L1 SSS FULL

     FILE 'HCAPLUS' ENTERED AT 17:50:19 ON 02 MAY 2007
L4           44 S L3/P
L5           14 S SALT? AND L4
                E US20050234129/PRN,PN,AN
                E US200500234129/PRN,PN,AN
                E NATEGLINIDE+ALL/CT
L6            0 S SALT? (W) NATEGLINIDE
L7            1 S "NATEGLINIDE SALT?"
                E US2005234129/PRN,PN,AN

     FILE 'STNGUIDE' ENTERED AT 18:00:24 ON 02 MAY 2007
L8            0 S  105816-04-4/RN OR 592523-31-4/RN OR 592523-32-5/RN OR 592524

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L9            9 S  105816-04-4/RN OR 592523-31-4/RN OR 592523-32-5/RN OR 592524
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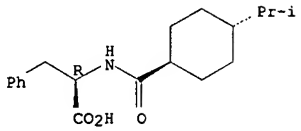
L9 ANSWER 1 OF 9 REGISTRY COPYRIGHT 2007 ACS on STN
RN 594837-89-5 REGISTRY
ED Entered STN: 29 Sep 2003
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, ammonium salt (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C19 H27 N O3 . x H3 N
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
CRN (105816-04-4)

Absolute stereochemistry.



●x NH3

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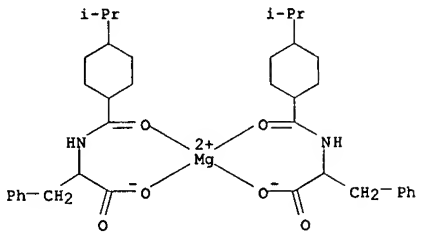
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L9 ANSWER 2 OF 9 REGISTRY COPYRIGHT 2007 ACS on STN
RN 594837-88-4 REGISTRY
ED Entered STN: 29 Sep 2003
CN Magnesium, bis[N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl- κO]-D-phenylalaninato-κO]-, (T-4)- (9CI) (CA INDEX NAME)
MF C38 H52 Mg N2 O6
CI CCS
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



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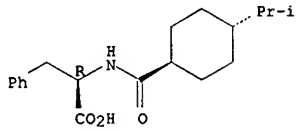
L9 ANSWER 3 OF 9 REGISTRY COPYRIGHT 2007 ACS on STN
RN 594837-87-3 REGISTRY
ED Entered STN: 29 Sep 2003
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, calcium salt (2:1) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C19 H27 N O3 . 1/2 Ca
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
CRN (105816-04-4)

Absolute stereochemistry.



●1/2 Ca

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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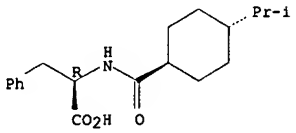
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L9 ANSWER 4 OF 9 REGISTRY COPYRIGHT 2007 ACS on STN
RN 594837-86-2 REGISTRY
ED Entered STN: 29 Sep 2003
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, monopotassium salt (9CI) (CA INDEX NAME)
FS STEREOSEARCH

MF C19 H27 N O3 . K
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
CRN (105816-04-4)

Absolute stereochemistry.



● K

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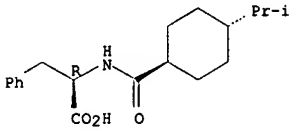
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L9 ANSWER 5 OF 9 REGISTRY COPYRIGHT 2007 ACS on STN
RN 594837-85-1 REGISTRY
ED Entered STN: 29 Sep 2003
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, monosodium salt (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C19 H27 N O3 . Na
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
CRN (105816-04-4)

Absolute stereochemistry.



● Na

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

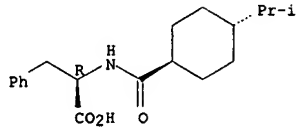
L9 ANSWER 6 OF 9 REGISTRY COPYRIGHT 2007 ACS on STN

RN 592524-24-8 REGISTRY
ED Entered STN: 25 Sep 2003
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with L-lysine (1:1) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C19 H27 N O3 . C6 H14 N2 O2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

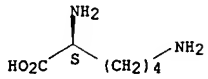
Absolute stereochemistry.



CM 2

CRN 56-87-1
CMF C6 H14 N2 O2

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

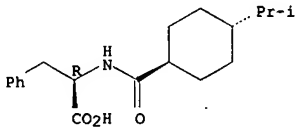
L9 ANSWER 7 OF 9 REGISTRY COPYRIGHT 2007 ACS on STN
RN 592523-32-5 REGISTRY
ED Entered STN: 25 Sep 2003
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with 2-amino-2-(hydroxymethyl)-1,3-propanediol (1:1) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C19 H27 N O3 . C4 H11 N O3
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

CM 1

CRN 105816-04-4

CMF C19 H27 N O3

Absolute stereochemistry.



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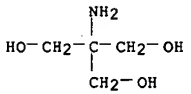
CRN 77-86-1
CMF C4 H11 N O3



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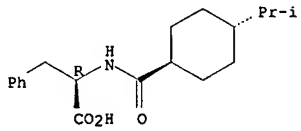
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L9 ANSWER 8 OF 9 REGISTRY COPYRIGHT 2007 ACS on STN
RN 592523-31-4 REGISTRY
ED Entered STN: 25 Sep 2003
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with 1-deoxy-1-(methylamino)-D-glucitol (1:1) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C19 H27 N O3 . C7 H17 N O5
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

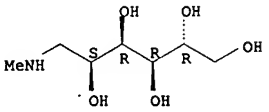
Absolute stereochemistry.



CM 2

CRN 6284-40-8
CMF C7 H17 N O5

Absolute stereochemistry.

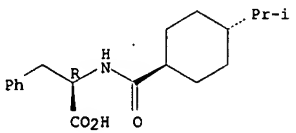


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L9 ANSWER 9 OF 9 REGISTRY COPYRIGHT 2007 ACS on STN
RN 105816-04-4 REGISTRY
ED Entered STN: 21 Dec 1986
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN D-Phenylalanine, N-[[4-(1-methylethyl)cyclohexyl]carbonyl]-, trans-
OTHER NAMES:
CN (-)-N-[(trans-4-Isopropylcyclohexyl)carbonyl]-D-phenylalanine
CN A 4166
CN AY 4166
CN D-Nateglinide
CN DJN 608
CN Fastic
CN Nateglinide
CN SDZ-DJN 608
CN Senaglinide
CN Starlix
CN Starlix DS
CN Starsis
FS STEREOSEARCH
DR 418766-62-8
MF C19 H27 N O3
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOSIS, BIOTECHNO, CA, CABA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PATDPASPC, PHAR, PIRA, PROMT, PROUSDDR, PS, RTECS*, SCISEARCH, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

535 REFERENCES IN FILE CA (1907 TO DATE)
10 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
538 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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=> fil stng
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                      21.30     282.65

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                       0.00     -11.70

FILE 'STNGUIDE' ENTERED AT 18:06:38 ON 02 MAY 2007
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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Apr 27, 2007 (20070427/UP).

=> fil hcaplu
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.12     282.77

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                       0.00     -11.70

FILE 'HCAPLUS' ENTERED AT 18:07:36 ON 02 MAY 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1907 - 2 May 2007  VOL 146 ISS 19
FILE LAST UPDATED: 1 May 2007  (20070501/ED)

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 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d his

     (FILE 'HOME' ENTERED AT 17:49:04 ON 02 MAY 2007)

     FILE 'REGISTRY' ENTERED AT 17:49:18 ON 02 MAY 2007
L1             STRUCTURE UPLOADED
L2           5 S L1 SSS SAM
L3          82 S L1 SSS FULL

     FILE 'HCAPLUS' ENTERED AT 17:50:19 ON 02 MAY 2007
L4          44 S L3/P
L5          14 S SALT? AND L4
               E US20050234129/PRN,PN,AN
               E US2005002341 29/PRN,PN,AN
               E NATEGLINIDE+ALL/CT
L6           0 S SALT? (W) NATEGLINIDE
L7           1 S "NATEGLINIDE SALT?"
               E US2005234129/PRN,PN,AN

     FILE 'STNGUIDE' ENTERED AT 18:00:24 ON 02 MAY 2007
L8           0 S  105816-04-4/RN OR 592523-31-4/RN OR 592523-32-5/RN OR 592524

     FILE 'REGISTRY' ENTERED AT 18:04:27 ON 02 MAY 2007
L9           9 S  105816-04-4/RN OR 592523-31-4/RN OR 592523-32-5/RN OR 592524

     FILE 'STNGUIDE' ENTERED AT 18:06:38 ON 02 MAY 2007

     FILE 'HCAPLUS' ENTERED AT 18:07:36 ON 02 MAY 2007

=> d l4 1-44 ibib abs

L4   ANSWER 1 OF 44  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:        2007:14393  HCAPLUS
DOCUMENT NUMBER:         146:163387
TITLE:                   Preparation of H type nateglinide crystal
INVENTOR(S):             Chen, Songnian; Feng, Qianjian; Yu, Yingmin
PATENT ASSIGNEE(S):      Hangzhou Pollen Co., Ltd., Peop. Rep. China
SOURCE:                  Faming Zhuanli Shenqing Gongkai Shuomingshu, 5pp.
                         CODEN: CNXXEV
DOCUMENT TYPE:           Patent
LANGUAGE:                Chinese
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ----------          ----   --------    --------------------   --------
     CN 1887858           A     20070103    CN 2006-10052617       20060721
PRIORITY APPLN. INFO.:                     CN 2006-10052617       20060721
OTHER SOURCE(S):         CASREACT 146:163387
AB   The title method comprises the steps of: (1) condensing
     trans-4-isopropylcyclohexanecarbonyl chloride with D-phenylalanine to
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obtain crude crystal of B type nateglinide, (2) dissolving the crude crystal in the solution of methanol, aminomethane and water (volume ratio of 60:20:20), heating to 40-60°C, adding 2% active carbon, decoloring for 7-15 min, filtrating, cooling to 10°C to precipitate, filtrating, washing with 40% ethanol till neutral, and drying to obtain H type nateglinide crystal, and (3) recrystg. the mother solution to obtain H type nateglinide crystal. The product of H type nateglinide crystal has good physiol. activity.

L4 ANSWER 2 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:657506 HCAPLUS
DOCUMENT NUMBER: 145:103952
TITLE: Process for the preparation of nateglinide, preferably in B-form
INVENTOR(S): Vigano, Enrico; Pizzatti, Enrica; Lanfranconi, Simona; Molteni, Renato; Landonio, Ernesto
PATENT ASSIGNEE(S): Italy
SOURCE: U.S. Pat. Appl. Publ., 22 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006148902	A1	20060706	US 2005-28283	20050103

PRIORITY APPLN. INFO.: US 2005-28283 20050103
OTHER SOURCE(S): CASREACT 145:103952
AB The invention relates to a process for the preparation of nateglinide, preferably in B-form, substantially free from the H-form, comprising three steps starting from (i) reaction in an organic solvent between D-phenylalanine Me ester or a salt and trans-4-isopropylcyclohexancarboxylic acid in the presence of an acyl chloride or carbonyldiimidazole, optionally isolating the nateglinide Me ester obtained and re-dissolving it in a second organic solvent, (ii) addition of water and alkali hydroxide to the reaction mixture and separation of the aqueous phase containing the alkali salt of nateglinide, and (iii) addition of hydrochloric acid to the aqueous phase from step (ii) to obtain nateglinide. In an example, the reaction was carried out in acetone in the presence of triethylamine and Et chloroformate and hydrolysis of nateglinide Me ester was carried out using toluene, tricaprylmethylammonium chloride, and aqueous potassium hydroxide to afford nateglinide in B-form (130.44°C).

L4 ANSWER 3 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:328161 HCAPLUS
DOCUMENT NUMBER: 145:173833
TITLE: Direct separation and enantioseparation of nateglinide stereoisomers by HPLC
AUTHOR(S): Yin, Yanjie; Zhang, Qiming; Li, Huiyi; Ning, Baoming; Liu, Wenying; Tian, Songjiu
CORPORATE SOURCE: China Pharmaceutical University, Nanjing, 210009, Peop. Rep. China
SOURCE: Yaowu Fenxi Zazhi (2005), 25(6), 657-659
CODEN: YFZADL; ISSN: 0254-1793
PUBLISHER: Yaowu Fenxi Zazhi Bianji Weiyuanhui
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB An HPLC method was developed to sep. the enantiomers of nateglinide as well as trans-nateglinide and cis-nateglinide. The nateglinide enantiomers, trans-nateglinide and cis-nateglinide were directly separated on a HPLC chiral stationary phase consisting of the Kromasil TBB with hexane-2-propanol-acetic acid (95:5:0.2) as eluent and a flow rate of 0.6 mL·min-1 at 258 nm and 20°C. Three kinds of Nateglinide could be completely separated, and the resolns. were 2.38 and 1.85, resp. The method can be used for separating the nateglinide enantiomers, trans-nateglinide and cis-nateglinide and determining content of nateglinide.

L4 ANSWER 4 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1328488 HCAPLUS
DOCUMENT NUMBER: 144:51894
TITLE: One-pot process for the preparation of nateglinide
INVENTOR(S): Kankan, Rajendra Narayanrao; Rao, Dharmaraj Ramachandra; Singh, Manjinder; Birari, Dilip Ramdas
PATENT ASSIGNEE(S): Cipla Limited, India; Wain, Christopher Paul
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005121071	A1	20051222	WO 2005-GB2267	20050608
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005252002	A1	20051222	AU 2005-252002	20050608
CA 2570041	A1	20051222	CA 2005-2570041	20050608
EP 1765769	A1	20070328	EP 2005-750279	20050608
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				

PRIORITY APPLN. INFO.: GB 2004-13084 A 20040611
WO 2005-GB2267 W 20050608
OTHER SOURCE(S): CASREACT 144:51894; MARPAT 144:51894
AB A one-pot process for the preparation of nateglinide is presented which comprises amidation of a C1-4 alkyl ester of D-phenylalanine, either as the free base or in salt form (typically the hydrochloride), with trans-4-isopropylcyclohexanecarboxylic acid or its acid halides to obtain a C1-4 alkyl ester of nateglinide, preferably the Me ester of nateglinide, followed by alkali (e.g., NaOH) saponification and acidification (e.g., HCl) to yield nateglinide (m.p. 128-131°).
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1261034 HCAPLUS

DOCUMENT NUMBER: 144:23128
TITLE: Stable nateglinide form b compositions via crystallization
INVENTOR(S): Venkataraman, Sundaram; Narsapur, Sharat Pandurang; Kharkar, Manoj Ramesh; Bangarubabu, Rongali; Sandeep, Mohanty; Sayantani, Pyne; Raju, Kakarlapudi Ranga
PATENT ASSIGNEE(S): Dr. Reddy's Laboratories Ltd., India; Dr. Reddy's Laboratories, Inc.
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005113485	A2	20051201	WO 2005-US17664	20050520

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-572689P P 20040520
US 2004-586431P P 20040708
US 2005-644614P P 20050118

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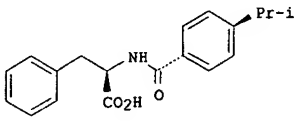


I

AB A process for preparing nateglinide Form B comprises dissolving nateglinide (I) in a solvent and adding the solution, at temps. of 40-45°C, to a hydrocarbon liquid that is at temps. of 40-45°C. Then, water is added and the mixture is allowed to cool, producing crystals of nateglinide Form B.

L4 ANSWER 6 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1240947 HCAPLUS
DOCUMENT NUMBER: 144:11582
TITLE: Process for the preparation of polymorphic crystalline forms of nateglinide ammonium salt
INVENTOR(S): Wizel, Shlomit; Frenkel, Gustavo; Gome, Boaz
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva

Pharmaceuticals Usa, Inc.
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005110972	A1	20051124	WO 2005-US16343	20050509

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2563793	A1	20051124	CA 2005-2563793	20050509
US 2006004102	A1	20060105	US 2005-126050	20050509
EP 1656339	A1	20060517	EP 2005-748381	20050509

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU

CN 1950331	A	20070418	CN 2005-80014509	20050509

PRIORITY APPLN. INFO.: US 2004-569047P P 20040507
WO 2005-US16343 W 20050509

AB Anti-hyperglycemic polymorphic crystalline forms of nateglinide ammonium salt are prepared
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:841495 HCAPLUS
DOCUMENT NUMBER: 145:315230
TITLE: Synthesis of nateglinide analogs and their bioactivity determination
AUTHOR(S): Zhang, Jianxin; Dong, Junjun; Han, Han; Gong, Zehui; Huang, Shijie; Liu, Keliang
CORPORATE SOURCE: Institute of Pharmacology and Toxicology, Academy of Military Medical Sciences, Beijing, 100850, Peop. Rep. China
SOURCE: Zhongguo Yaowu Huaxue Zazhi (2004), 14(6), 335-339, 362
CODEN: ZYHZEF; ISSN: 1005-0108
PUBLISHER: Zhongguo Yaowu Huaxue Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
OTHER SOURCE(S): CASREACT 145:315230
AB Analogs of nateglinide [i.e., N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-D-phenylalanine] were synthesized, and their biol. activities were tested by glycemia levels in mice. The new compds. were synthesized using N-(isopropyl)piperazine, N-isopropyl-4-piperidinecarboxylic acid, trans-4-dimethylamino-1-cyclohexanecarboxylic acid and substituted

phenylalanine as the starting materials. The biol. activities of the new compds. were tested by the glycemia levels in mice via drug administration after forbiddance of food-intake and oral delivery of glucose. Forty-three new compds. were synthesized, and their structures were confirmed by elementary anal., IR, polarimetric anal., 1H-NMR and MS. One compound, 4-fluoro-N-[[4-(1-methylethyl)-1-piperazinyl]carbonyl]-L-phenylalanine monohydrochloride, showed significant hypoglycemic effect on glycemia of mice, and had an (S)-configuration at the chiral center, which was opposite to the control.

L4 ANSWER 8 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:476519 HCAPLUS
DOCUMENT NUMBER: 143:97635
TITLE: Improved process for the preparation of hypoglycemic agent nateglinide
INVENTOR(S): Zhong, Bohua; Wu, Bo; Yan, Yuan
PATENT ASSIGNEE(S): Toxic Drug Inst., Academy of Military Medical Science, PLA, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, No pp. given
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1517335	A	20040804	CN 2003-100559	20030117

PRIORITY APPLN. INFO.: CN 2003-100559 20030117
OTHER SOURCE(S): CASREACT 143:97635
AB A scalable process for the preparation of nateglinide, a hypoglycemic agent, was reported. The key improvement is that the acylation of D-phenylalanine with 4-isopropylcyclohexanecarbonyl chloride was performed under a homogeneous condition using a mixture of dioxane or THF and H2O as solvent, largely increasing the yield. Other features include the use of cheap Pd/C instead of previously expensive PtO2 as hydrogenation catalyst in the reduction of 4-isopropylbenzoic acid into 4-isopropylcyclohexanecarboxylic acid. Purification of nateglinide by recrystn. in petroleum ether, hexane and cyclohexane or their mixts. is claimed.

L4 ANSWER 9 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:476518 HCAPLUS
DOCUMENT NUMBER: 143:26875
TITLE: Improved process for the preparation of hypoglycemic agent nateglinide
INVENTOR(S): Zhu, Qin; Pan, Junfang; Shi, Mingfeng
PATENT ASSIGNEE(S): Shanghai Huashuo Medicine Science & Technology Development Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, No pp. given
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

CN 1517334	A	20040804	CN 2003-114970	20030117

PRIORITY APPLN. INFO.: CN 2003-114970 20030117
OTHER SOURCE(S): CASREACT 143:26875
AB A scalable process for the preparation of nateglinide, a hypoglycemic agent, was reported. The key improvement is that the acylation of D-phenylalanine with 4-isopropylcyclohexanecarbonyl chloride was performed under a homogeneous condition using a mixture of DMF and H2O as solvent, largely increasing the yield. Other features include the use of cheap Pd/C instead of previously expensive PtO2 as hydrogenation catalyst in the reduction of 4-isopropylbenzoic acid into 4-isopropylcyclohexanecarboxylic acid.

L4 ANSWER 10 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:467801 HCAPLUS
DOCUMENT NUMBER: 143:7982
TITLE: Process for the preparation of the crystalline B-form nateglinide from D-phenylalanine methyl ester and trans-4-isopropylcyclohexanecarboxylic acid
INVENTOR(S): Vigano', Enrico; Pizzati, Enrica; Lanfranconi, Simona; Molteni, Renato; Landonio, Ernesto
PATENT ASSIGNEE(S): A.M.S.A. Anonima Materie Sintetiche e Affini S.p.A., Italy
SOURCE: Eur. Pat. Appl., 32 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1535900	A1	20050601	EP 2003-27114	20031126
EP 1535900	B1	20061227		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 349418	T	20070115	AT 2003-27114	20031126

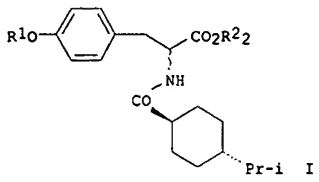
PRIORITY APPLN. INFO.: EP 2003-27114 A 20031126
OTHER SOURCE(S): CASREACT 143:7982
AB A process for the preparation of nateglinide comprises: (I) the amidation reaction in a first organic solvent between D-phenylalanine Me ester, or a salt, and trans-4-isopropylcyclohexanecarboxylic acid and an acyl chloride, or carbonyldiimidazole, to obtain the nateglinide Me ester; (Ia) optionally isolating the nateglinide Me ester and redissolving it in a second organic solvent to give a solution; (II) addition of water and alkali hydroxide to the reaction mixture coming from step (I) without isolating the nateglinide Me ester, or, if applicable, to the solution of step (Ia), and separation of the aqueous phase containing the alkali salt of nateglinide; (III) addition of hydrochloric acid to the aqueous phase coming from step (II) to obtain nateglinide , wherein the organic solvent employed in step (II) is a water non-miscible solvent.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:414565 HCAPLUS
DOCUMENT NUMBER: 142:482315
TITLE: Preparation of alanine derivative as antidiabetics
INVENTOR(S): Yang, Yushe; Tang, Lei; Ji, Ruyun; Chen, Kaixian

PATENT ASSIGNEE(S): Shanghai Institute of Pharmacy, Chinese Academy of Sciences, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 26 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1431197	A	20030723	CN 2003-115160	20030124
PRIORITY APPLN. INFO.:			CN 2003-115160	20030124

OTHER SOURCE(S): CASREACT 142:482315; MARPAT 142:482315
GI



I

AB Alanine derivs. I (R1 = 2-(1-indolyl)ethyl, 2-[N-(2-benzoxazolyl)-N-methyl]aminoethyl, 2-{N-methyl-N-(2-pyridinyl)]aminoethyl, 2-(4-methyl-2-phenyl-4-oxazolyl)ethyl, 4-trifluoromethylbenzyl, benzyl; R2 = H, alkyl) is prepared by condensation reaction of trans-4-isopropylcyclohexanecarboxylic acid N-succinimidyl ester with L- or D-tyrosine Me ester in inert solvent to obtain 3-(4-hydroxyphenyl)-2-(trans-isopropylcyclohexylcarboxamido)propanoic acid Me ester (II), Mitsunobu reaction with aromatic alc., and then hydrolysis with inorg. base solution The method may be prepared by (1) etherification of II with alkyl halide in alkaline medium; (2) hydrolysis of II; or (3) condensation reaction of II with amino-protected 2-methylaminoethanol, condensation reaction with 2-fluoropyridine, and hydrolysis with base. The alanine derivative and its salt may be used to prepare the medical prepns. for treating type II diabetes mellitus.

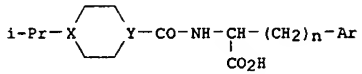
L4 ANSWER 12 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:249676 HCAPLUS
DOCUMENT NUMBER: 144:88520
TITLE: Syntheses and hypoglycemia activities of N-(trans-4-isopro-pylcyclohexylcarbonyl)-β-ring substituted phenylalanines
AUTHOR(S): Pan, Man-gen; Liang, Yuan-jun; Li, Bi-hai; Zhong, Bo-hua; Huang, Shi-jie; Gong, Ze-hui; Liu, Ke-liang
CORPORATE SOURCE: Institute of Pharmacology and Toxicology, Academy of Military Medical Sciences, Beijing, 100850, Peop. Rep. China
SOURCE: Zhongguo Yaowu Huaxue Zazhi (2003), 13(5), 249-253

CODEN: ZYHZEF; ISSN: 1005-0108
PUBLISHER: Zhongguo Yaowu Huaxue Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
OTHER SOURCE(S): CASREACT 144:88520
AB A series of title compds. were synthesized as nateglinide (N-(trans-4-isopropylcyclohexyl-1-carbonyl)-D-phenylalanine) analogs by condensation of substituted phenylalanine derivs. with trans-4-isopropylcyclohexanecarbonyl chloride. 3-Fluoro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-L-phenylalanine was prepared and showed hypoglycemic activity comparable to that of nateglinide.

L4 ANSWER 13 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:204069 HCAPLUS
DOCUMENT NUMBER: 142:482313
TITLE: Preparation of aromatic amino acid derivatives for treatment of blood sugar disorders
INVENTOR(S): Liu, Keliang; Pan, Mangen; Liang, Yuanjun; Zhong, Bohua; Li, Bihai; Huang, Shijie; Li, Xin; Dong, Huajin; Chi, Mugen
PATENT ASSIGNEE(S): Institute of Toxicant and Pharmaceuticals, Academy of Military Medical Science of PLA, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 41 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1453265	A	20031105	CN 2003-123272	20030425
PRIORITY APPLN. INFO.:			CN 2002-116715 A	20020426

OTHER SOURCE(S): CASREACT 142:482313; MARPAT 142:482313
GI



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AB The aromatic amino acid derivs. I [n = 0, 1; X, Y = C, N; Ar = benzene ring substituted by one or more substituents (such as halo, NO2, OH, CO2H, CF3, trifluoromethoxy, methylenedioxy, methylenedithio, alkyl, alkenyl, cycloalkyl, cycloalkenyl, aryl, alkoxy, alkenoxy, phenoxy, benzyloxy, ester group, amino, amido), other aromatic ring, heterocyclic ring or its substituted derivative], useful for the treatment of blood sugar disorders, were prepared by acylation of 3-arylalanine HCl with 4-isopropylcyclohexylcarbonyl chloride or 1-isopropyl-4-piperidinylcarbonyl chloride. Thus, reaction of D-3-nitrophenylalanine hydrochloride with trans-4-isopropylcyclohexanecarbonyl chloride in THF in the presence of aqueous NaOH at room temperature for 5 h gave, after acidification with aqueous HCl, 71.1% N-(trans-4-isopropylcyclohexanecarbonyl)-D-3-nitrophenylalanine (II). II showed endothelin receptor antagonist activity at 10-9mol/L.

L4 ANSWER 14 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:59980 HCAPLUS
DOCUMENT NUMBER: 142:141289
TITLE: Crystalline form of nateglinide
INVENTOR(S): Frenkel, Gustavo; Gome, Boaz; Wizel, Shlomit
PATENT ASSIGNEE(S): Israel
SOURCE: U.S. Pat. Appl. Publ., 91 pp., Cont.-in-part of U.S. Ser. No. 622,905.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005014836	A1	20050120	US 2003-746697	20031224
US 2004181089	A1	20040916	US 2003-622905	20030718
CA 2513753	A1	20040812	CA 2004-2513753	20040113
WO 2004067496	A1	20040812	WO 2004-US839	20040113
WO 2004067496	A9	20041209		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
EP 1511717	A1	20050309	EP 2004-701826	20040113
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1835912	A	20060920	CN 2004-80005672	20040113
US 2007004804	A1	20070104	US 2006-516363	20060905
PRIORITY APPLN. INFO.:			US 2003-442109P	P 20030123
			US 2003-449791P	P 20030224
			US 2003-479016P	P 20030616
			US 2003-622905	A2 20030718
			US 2002-396904P	P 20020718
			US 2002-413622P	P 20020925
			US 2002-414199P	P 20020926
			US 2002-423750P	P 20021105
			US 2002-432093P	P 20021210
			US 2002-432962P	P 20021212
			US 2003-622999	A1 20030718
			WO 2003-US22375	A 20030718
			US 2003-693166	A 20031023
			US 2003-746697	A 20031224
			WO 2004-US839	W 20040113

AB Crystalline forms of nateglinide and processes for their preparation, as well as pharmaceutical formulations containing them and methods of administration are provided. A process for preparing crystalline form of nateglinide comprises the steps of(a) preparing a solution of nateglinide in Et acetate, (b) seeding the solution with nateglinide crystals, and (c) recovering the crystalline form as a precipitate The nateglinide obtained is more than about 99% pure. For example, nateglinide (5 g) was dissolved in acetonitrile, acetone, or Et acetate at about 55° in over about 15 min until a clear solution was obtained. The solvent was removed to dryness by evaporation at about 55°/20 to 30 mmHg to give dry nateglinide crystalline Form B. Also, nateglinide Form Z was

prepared by treating 7.73 g of D-phenylalanine (PheOH) with 185 mL (3.5 equiv) of 3.5% NaOH at room temperature to afford a clear solution of the corresponding Na-salt. A solution of neat trans-4-isopropylcyclohexanecarboxyl chloride (IPCHAC, 9.02 g, 1.01 equiv) was added to the solution of Phe-OH obtained above, over 3 min, while stirring at room temperature The rest of the IPCHAC in the funnel was washed with toluene (1 mL) and added. The resulting mixture was stirred for 1 h, and was treated with 10% HCl (32 mL) to adjust the pH to 3, while stirring. The mixture was stirred for 1 h, and filtered. The solid was washed with water (200 mL) and sucked well to afford 33.3 g of the moist product, which lost weight after drying at 78°/2.2 mbar (Assay 98.4%, purity >99% , yield 86%).

L4 ANSWER 15 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:55192 HCAPLUS
DOCUMENT NUMBER: 142:156316
TITLE: A saponification and neutralization process for the preparation of chirally pure nateglinide from its lower alkyl esters and nateglinide polymorphic crystalline modifications
INVENTOR(S): Gazdag, Maria; Gizur, Tibor; Hegedus, Bela; Szemzo, Attila; Tarkanyi, Gabor; Toerley, Jozsef; Babjak, Monika
PATENT ASSIGNEE(S): Richter Gedeon Vegyeszeti Gyar Rt., Hung.
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005005373	A1	20050120	WO 2004-HU73	20040708
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
HU 200302174	A2	20050728	HU 2003-2174	20030710
EP 1651591	A1	20060503	EP 2004-743732	20040708
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR				
US 2007043117	A1	20070222	US 2006-564017	20060515
PRIORITY APPLN. INFO.:			HU 2003-2174	A 20030710
			WO 2004-HU73	W 20040708

OTHER SOURCE(S): CASREACT 142:156316
AB The preparation of chirally pure nateglinide by treating a nateglinide lower alkyl ester (e.g., Me ester) with an alkali base (e.g., sodium hydroxide) to yield an alkali salt and neutralizing liberating the salt by addition of an acid (e.g., aqueous HCl) is described as is the preparation of polymorphic crystalline modifications of nateglinide.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:937572 HCAPLUS
DOCUMENT NUMBER: 142:317044
TITLE: An efficient large scale synthesis of nateglinide
AUTHOR(S): Chandrasekhar, Batchu; Sawanth, Mangesh S.; Naik, Sameer J.; Gaikwad, Nandakumar B.; Kulkarni, Pramila V.; Bhirud, Shekar B.
CORPORATE SOURCE: Process Research and Development, Glenmark Research Centre, MIDC Mahape, Navi Mumbai, 400709, India
SOURCE: Organic Preparations and Procedures International (2004), 36(5), 459-467
CODEN: OPPIAK; ISSN: 0030-4948
PUBLISHER: Organic Preparations and Procedures, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:317044
AB Nateglinide was prepared as the desired H polymorph by reaction of trans-4-isopropylcyclohexanecarboxylic acid with ClCO2Et and treating the carbonate with D-phenylalanine.
REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:648495 HCAPLUS
DOCUMENT NUMBER: 141:157476
TITLE: Preparation of alanine compounds as antidiabetics
INVENTOR(S): Yang, Yushe; Tang, Lei; Ji, Ruyun; Chen, Kaixian
PATENT ASSIGNEE(S): Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Peop. Rep. China
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004067495	A1	20040812	WO 2003-CN96	20030128
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003303815	A1	20040823	AU 2003-303815	20030128
EP 1591440	A1	20051102	EP 2003-815509	20030128
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006513250	T	20060420	JP 2004-567216	20030128
US 2006154970	A1	20060713	US 2005-543091	20050722
PRIORITY APPLN. INFO.:			WO 2003-CN96 A	20030128
OTHER SOURCE(S):	CASREACT 141:157476; MARPAT 141:157476			

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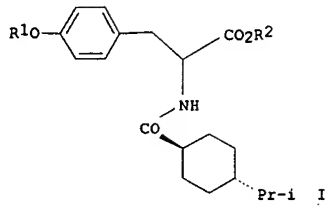


AB Alanine compds. I (R1 = H, alkyl, Ph, aryl, heteroaryl, etc.; R2 = H, alkyl), useful for treatment of type II diabetes, are prepared Thus, (2S)--2-[N-(trans-4-isopropylcyclohexylcarbonyl)amino]-3-[4-[2-(5-methyl-2-phenyl-4-oxazolyl)ethoxy]phenyl]propionic acid was prepared and showed insulin sensitizer activity.

L4 ANSWER 18 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:203799 HCAPLUS
DOCUMENT NUMBER: 140:241062
TITLE: Process for the formation of a crystalline polymorphic form of nateglinide
INVENTOR(S): Reguri, Buchi Reddy; Kadaboina, Rajasekhar; Polavarapu, Srinivas
PATENT ASSIGNEE(S): Reddy's Laboratories Limited, India; Reddy's Laboratories, Inc.
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004020396	A1	20040311	WO 2003-US26880	20030827
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IN 2002MA00631	A	20050304	IN 2002-MA631	20020828
AU 2003262928	A1	20040319	AU 2003-262928	20030827
US 2004077725	A1	20040422	US 2003-649380	20030827
PRIORITY APPLN. INFO.:			IN 2002-MA631 A	20020828
			WO 2003-US26880 W	20030827

AB A crystalline polymorphic form of nateglinide are described and its X-ray diffraction pattern presented.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 19 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:203709 HCAPLUS
DOCUMENT NUMBER: 140:259085
TITLE: Preparation of nateglinide inclusion complexes with cyclodextrins and their use in pharmaceutical compositions
INVENTOR(S): Niu, Zhanqi; Wang, Lifang; Chen, Yujie; Shen, Dongmin
PATENT ASSIGNEE(S): Zhongqi Pharmaceutical Technology (Shijiazhuang) Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004019989	A1	20040311	WO 2003-CN707	20030822
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 1478470	A	20040303	CN 2002-132321	20020827
AU 2003255130	A1	20040319	AU 2003-255130	20030822
PRIORITY APPLN. INFO.:			CN 2002-132321 A	20020827
			WO 2003-CN707 W	20030822

AB The invention relates to preparation of inclusion complexes of nateglinide, containing nateglinide and β-cyclodextrin and its derivates, particularly to nateglinide-β-cyclodextrin inclusion complexes. The preparing process comprises saturated solution method, ultrasonic method and grinding method. The inclusion complexes obtained have high stability and can be used in the manufacture of pharmaceutical formulations of nateglinide. For example, nateglinide-β-cyclodextrin (1:2) inclusion complex prepared by grinding the mixture of 10 mL nateglinide (0.0031 mol) ethanol solution and 7g β-cyclodextrin (0.0062 mol), was incorporated into tablets together with starch, crosslinked CMC and magnesium stearate.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:182826 HCAPLUS
DOCUMENT NUMBER: 140:199745
TITLE: Synthesis and purification of nateglinide
INVENTOR(S): Naik, Samir Jaivant; Kulkarni, Pramila Vijay; Gaikwad, Nandkumar Baburao; Sawant, Mangesh Shivram; Bhirud, Shekhar; Batchu, Chandrasekhar
PATENT ASSIGNEE(S): Glenmark Pharmaceuticals Limited, India
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004018408	A1	20040304	WO 2003-IB3270	20030812
WO 2004018408	A8	20050310		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IN 2002MU00773	A	20040605	IN 2002-MU773	20020826
AU 2003263386	A1	20040311	AU 2003-263386	20030812
PRIORITY APPLN. INFO.:			IN 2002-MU773 A	20020826
			WO 2003-IB3270 W	20030812

OTHER SOURCE(S): CASREACT 140:199745; MARPAT 140:199745
AB N-[(trans-4-isopropylcyclohexyl)carbonyl]-D-phenylalanine (nateglinide) was prepared by reaction of trans-4-isopropylcyclohexylcarboxylic acid with an alkyl chloroformate in a ketonic solvent in the presence of a base at -20 to 30°C and reaction of the mixed anhydride product with an aqueous alkali salt solution of D-phenylalanine. An example shows the synthesis of nateglinide by using triethylamine and Et chloroformate in acetone (97% pure following HPLC).
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 21 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:80637 HCAPLUS
DOCUMENT NUMBER: 140:151932
TITLE: Preparation of polymorphic forms of nateglinide
INVENTOR(S): Yahalomi, Ronit; Shapior, Evgeny; Dolitzky, Ben-zion; Gozlan, Yigael; Gome, Boaz
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceutical Usa, Inc.
SOURCE: PCT Int. Appl., 130 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004009532	A1	20040129	WO 2003-US22375	20030718
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,				

KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004152782		A1	20040805	US 2003-614266	20030703
US 6861553		B2	20050301		
CA 2492644		A1	20040129	CA 2003-2492644	20030718
AU 2003253971		A1	20040209	AU 2003-253971	20030718
US 2004116526		A1	20040617	US 2003-623237	20030718
US 7148376		B2	20061212		
EP 1467964		A1	20041020	EP 2003-765665	20030718
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005014949		A1	20050120	US 2003-623290	20030718
US 2005075400		A1	20050407	US 2003-622999	20030718
CN 1723190		A	20060118	CN 2003-821921	20030718
JP 2006511614		T	20060406	JP 2005-505521	20030718
CA 2513753		A1	20040812	CA 2004-2513753	20040113
WO 2004067496		A1	20040812	WO 2004-US839	20040113
WO 2004067496		A9	20041209		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
EP 1511717		A1	20050309	EP 2004-701826	20040113
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1835912		A	20060920	CN 2004-80005672	20040113
US 2007004804		A1	20070104	US 2006-516363	20060905

PRIORITY APPLN. INFO.:	US 2002-396904P	P	20020718
	US 2002-413622P	P	20020925
	US 2002-414199P	P	20020926
	US 2002-423750P	P	20021105
	US 2002-432093P	P	20021210
	US 2002-432962P	P	20021212
	US 2003-442109P	P	20030123
	US 2003-449791P	P	20030224
	US 2003-479016P	P	20030616
	US 2003-614266	A	20030703
	US 2002-393495P	P	20020703
	US 2003-622905	A	20030718
	US 2003-622999	A1	20030718
	WO 2003-US22375	W	20030718
	US 2003-693166	A	20031023
	US 2003-746697	A	20031224
	WO 2004-US839	W	20040113

AB The invention discloses the preparation of 26 characterized forms of nateglinide (forms A, C, D, F, G, I, J, K, L, M, N, O, P, Q, T, U, V, Y, α, β, γ, δ, ε, σ, θ and Ω). Most of the forms are solvates (with the exception of forms L, P, U, α, δ and σ). Polymorphic forms are characterized by their mp, DSC, XRPD, FTIR; form interconversion is also discussed. For example, D-phenylalanine is reacted with trans-[[4-(isopropyl)cyclohexanee]carbonyl]chloride (i. NaOHaq; ii. H2SO4). The wet cake of nateglinide is dissolved in EtOAc, the aqueous phase is removed and the resulting solution heated to 50° under reduced pressure and added to hot heptane. The resulting solution is cooled and seeded with the B-form to afford the δ-form (33% yield).

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 22 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:41431 HCAPLUS
DOCUMENT NUMBER: 140:94292
TITLE: Process for preparing nateglinide and its intermediates
INVENTOR(S): Yahalomi, Ronit; Shapiro, Evgeny; Dolitzky, Ben-zion; Gozlan, Yigael
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals Usa, Inc.
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004005240	A1	20040115	WO 2003-US21238	20030703
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003256454	A1	20040123	AU 2003-256454	20030703
EP 1487782	A1	20041222	EP 2003-763310	20030703
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1671649	A	20050921	CN 2003-817439	20030703
US 2004116526	A1	20040617	US 2003-623237	20030718
US 7148376	B2	20061212		
US 2005014949	A1	20050120	US 2003-623290	20030718
US 2005075400	A1	20050407	US 2003-622999	20030718
CN 1723190	A	20060118	CN 2003-821921	20030718
US 2007004804	A1	20070104	US 2006-516363	20060905

PRIORITY APPLN. INFO.:	US 2002-393495P	P	20020703
	US 2002-396904P	P	20020718
	US 2002-413622P	P	20020925
	US 2002-414199P	P	20020926
	US 2002-423750P	P	20021105
	US 2002-432093P	P	20021210
	US 2002-432962P	P	20021212
	US 2003-442109P	P	20030123
	US 2003-449791P	P	20030224
	US 2003-479016P	P	20030616
	WO 2003-US21238	W	20030703
	US 2003-622999	A1	20030718

OTHER SOURCE(S): CASREACT 140:94292

AB A process for the preparation of nateglinide involves converting trans-4-isopropylcyclohexanecarboxylic acid into the acid chloride by reaction with thionyl chloride in the presence of an organic amide and acylation of a suitable salt of D-phenylalanine with the acid chloride in a single or two phase system or in water free of a co-solvent.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 23 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:892741 HCAPLUS
DOCUMENT NUMBER: 139:369757
TITLE: Process for the preparation of a crystal polymorphic form of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (nateglinide)
INVENTOR(S): Rajamahendra, Shanmughasamy; Aswathanarayanappa, Chandrashekar; Puthiaparampil, Tom Thomas; Sridharan, Madhavan; Ganesh, Sambasivam
PATENT ASSIGNEE(S): Biocon India Limited, India
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003093222	A1	20031113	WO 2002-IN114	20020429
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2481322	A1	20031113	CA 2002-2481322	20020429
AU 2002304281	A1	20031117	AU 2002-304281	20020429
EP 1499586	A1	20050126	EP 2002-733208	20020429
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
HU 200500259	A2	20050628	HU 2005-259	20020429
US 2005165108	A1	20050728	US 2003-508364	20020429
JP 2005523933	T	20050811	JP 2004-501362	20020429
PRIORITY APPLN. INFO.:			WO 2002-IN114 W	20020429

AB Novel polymorph Form C of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (I; i.e., nateglinide) is produced having a different IR spectrum and X-ray diffraction patterns (presented) from previously known forms of I.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 24 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:837030 HCAPLUS
DOCUMENT NUMBER: 139:341723
TITLE: Novel nateglinide crystals
INVENTOR(S): Koguchi, Yoshihito; Nakao, Tomoko; Sumikawa, Michito
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003087039	A1	20031023	WO 2003-JP4686	20030414
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003236243	A1	20031027	AU 2003-236243	20030414
EP 1496048	A1	20050112	EP 2003-746474	20030414
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005101672	A1	20050512	US 2004-965171	20041015
PRIORITY APPLN. INFO.:			JP 2002-111963 A	20020415
			WO 2003-JP4686 W	20030414

AB A type crystal (powder X-ray diffraction main peaks: 4.4°, 5.2°, 15.7°, 18.5° (2 theta)), M type crystal (powder X-ray diffraction main peaks: 6.0°, 14.2°, 15.2°, 18.8° (2 theta)), and P type crystal (powder X-ray diffraction main peaks: 4.8°, 5.3°, 14.3°, 15.2° (2 theta)) of nateglinide, which are all novel crystals, can be prepared by a method comprising dissolving nateglinide in a solvent exhibiting high solubility for nateglinide and then adding a solvent exhibiting poor solubility for nateglinide or dissolving nateglinide in a mixed solvent comprising a solvent exhibiting high solubility for nateglinide and a solvent exhibiting poor solubility for nateglinide and then cooling the resulting nateglinide solution to precipitate crystals, subjecting the product to filtration, and then drying at a specific temperature. Nateglinide is a known antidiabetic.
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 25 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:737716 HCAPLUS
DOCUMENT NUMBER: 139:230996
TITLE: Preparation and properties of nateglinide salts
INVENTOR(S): Sutton, Paul Allen; Vivilecchia, Richard Victor; Parker, David John; De La Cruz, Marilyn
PATENT ASSIGNEE(S): Novartis Ag, Switz.; Novartis Pharma Gmbh
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003076393	A1	20030918	WO 2003-EP2447	20030310
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,				

HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR

CA 2478599	A1	20030918	CA 2003-2478599	20030310
AU 2003214112	A1	20030922	AU 2003-214112	20030310
EP 1483232	A1	20041208	EP 2003-709769	20030310
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003008316	A	20041228	BR 2003-8316	20030310
JP 2005519949	T	20050707	JP 2003-574615	20030310
CN 1642904	A	20050720	CN 2003-805803	20030310
US 2005234129	A1	20051020	US 2004-507255	20040928
PRIORITY APPLN. INFO.:			US 2002-363178P P	20020311
			WO 2003-EP2447 W	20030310

AB The invention relates to salts of nateglinide having specified properties (m.ps., solubilities, X-ray diffraction patterns) for use in pharmaceutical compns. for preventing or treating diabetes, cardiovascular diseases, etc. Nateglinide Na, K, Ca, Mg, N-methyl-D-glucamine, TRIS, lysine, and ammonium salts were prepared and their properties tabulated.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 26 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:76738 HCAPLUS
DOCUMENT NUMBER: 138:137033
TITLE: Oxidative process and catalysts for the manufacture of para-substituted benzoic acids from their corresponding aldehydes
INVENTOR(S): Girgis, Michael John; Shekhar, Ratna
PATENT ASSIGNEE(S): Novartis AG, Switz.
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003008367	A2	20030130	WO 2002-US22631	20020716
WO 2003008367	A3	20030410		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003023115	A1	20030130	US 2002-196600	20020715
US 6740776	B2	20040525		
AU 2002313681	A1	20030303	AU 2002-313681	20020716
PRIORITY APPLN. INFO.:			US 2001-305648P P	20010716
			WO 2002-US22631 W	20020716

OTHER SOURCE(S): CASREACT 138:137033; MARPAT 138:137033
AB A low-temperature process for preparing aromatic acids 4-(R1R2CH)C6H4CO2H [R1, R2 = H, C1-8 (un)branched alkyl, cycloalkyl; e.g., 4-isopropylbenzoic acid] comprises oxidizing the corresponding aromatic aldehyde 4-(R1R2CH)C6H4CHO (e.g., 4-isopropylbenzaldehyde) with a gas having an oxygen content of 1-100% at 20° to <100° in the presence of a supported Group VIII metal catalyst (e.g., Pt/C), and using a solvent having a flash point >95°C and/or a m.p. <55°, provided that the flash point of the solvent is greater than the reaction temperature

L4 ANSWER 27 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:62632 HCAPLUS
DOCUMENT NUMBER: 138:73015
TITLE: Synthesis process for trans-4-isopropylcyclohexanecarboxylic acid
INVENTOR(S): Gu, Lianquan; An, Linkun; Ma, Lin; Guo, Xindong; Huang, Zhishu
PATENT ASSIGNEE(S): Zhongshan Univ., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 6 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1319583	A	20011031	CN 2001-107459	20010116
PRIORITY APPLN. INFO.:			CN 2001-107459	20010116

OTHER SOURCE(S): CASREACT 138:73015
AB The process comprises hydrogenating cumic acid in acetic acid in the presence of PtO2, recovering solvent, treating with 10-35% inorg. base (such as Ba(OH)2, Mg(OH)2, KOH, or NaOH) solution at 50-150° for 10-20 h, neutralizing with HCl to pH 2, crystallizing, filtering, and recrystg. in methanol.

L4 ANSWER 28 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:30017 HCAPLUS
DOCUMENT NUMBER: 139:210299
TITLE: Study on separation of cis-isomer of nateglinide by high-pressure liquid chromatographic method
AUTHOR(S): Yan, Xiaoyan; Hu, Xin; Cao, Guoying; He, Xiaorong; Yin, Qi
CORPORATE SOURCE: Beijing Hospital, Ministry of Public Health, Beijing, 100730, Peop. Rep. China
SOURCE: Zhongguo Yaoxue Zazhi (Beijing, China) (2002), 37(6), 444-446
CODEN: ZYZAEU; ISSN: 1001-2494
PUBLISHER: Zhongguo Yaoxue Zazhishe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB A high-pressure liquid chromatog. method for the separation of cis-isomer of nateglinide was established on Phenomenex Luna C18 column (5 μm, 4.6 mm x 250 mm) with UV detection at 214 nm and room temperature The mobile phase was consisted of (A) acetonitrile and (B) 0.03 mol L-1 phosphate buffer (pH 2.5, 65:35, volume/volume). The resolution factors were at least 1.5. The limits of detection and quantitation limit was 0.06 and 0.18 μg mL-1,

resp. The method is useful in separation and determination of the cis-isomer from nateglinide.

L4 ANSWER 29 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:609152 HCAPLUS
DOCUMENT NUMBER: 138:254901
TITLE: a new synthesis method of nateglinide as antidiabetic drug
AUTHOR(S): Wang, Dun; Liang, Yiheng; Gong, Ping; Zhao, Yanfang
CORPORATE SOURCE: School of Pharmaceutical Engineering, Shenyang Pharmaceutical University, Shenyang, 110016, Peop. Rep. China
SOURCE: Zhongguo Yaowu Huaxue Zazhi (2002), 12(2), 94-96
CODEN: ZYHZEF; ISSN: 1005-0108
PUBLISHER: Zhongguo Yaowu Huaxue Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
OTHER SOURCE(S): CASREACT 138:254901
AB A new antidiabetic drug-nateglinide was synthesized from isopropylbenzene by Friedel-Crafts reaction, chloroform reaction, catalytic hydrogenation to obtain trans-4-isopropylhexanecarboxylic acid, acylation of D-phenylalanine Et ester, hydrolysis to obtain nateglinide B-type crystal, and crystal-conversion. The total yield was 9.8%.

L4 ANSWER 30 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:332157 HCAPLUS
DOCUMENT NUMBER: 136:340998
TITLE: Process for producing B-form nateglinide crystals
INVENTOR(S): Sumikawa, Michito; Maruo, Makoto; Miyazaki, Kazuo; Nishina, Shigehiro; Matsuzawa, Yukiko
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: PCT Int. Appl., 9 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002034713	A1	20020502	WO 2001-JP9293	20011023
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 200196001	A	20020506	AU 2001-96001	20011023
CA 2426745	A1	20030423	CA 2001-2426745	20011023
EP 1334964	A1	20030813	EP 2001-976819	20011023
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001014846	A	20040225	BR 2001-14846	20011023
RU 2275354	C2	20060427	RU 2003-111948	20011023
US 2003229249	A1	20031211	US 2003-421888	20030424

IN 2003CN00609	A	20050415	IN 2003-CN609	20030424
PRIORITY APPLN. INFO.:			JP 2000-324375	A 20001024
			WO 2001-JP9293	W 20011023

AB A process for producing B-form nateglinide crystals containing substantially no H-form crystals comprises the steps of drying wet crystals of a nateglinide solvate at a low temperature until the solvent disappears and then causing them to undergo a crystal transition. Nateglinide is a known antidiabetic. By this process, B-form nateglinide crystals can be produced on an industrial scale.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 31 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:314896 HCAPLUS
DOCUMENT NUMBER: 136:325825
TITLE: Process for producing nateglinide crystals
INVENTOR(S): Takahashi, Daisuke; Nishi, Seiichi; Takahashi, Satoji
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002032854	A1	20020425	WO 2001-JP9069	20011016
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 200194265	A	20020429	AU 2001-94265	20011016
CA 2425538	A1	20030410	CA 2001-2425538	20011016
EP 1334963	A1	20030813	EP 2001-974875	20011016
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001014729	A	20031014	BR 2001-14729	20011016
RU 2273629	C2	20060410	RU 2003-111021	20011016
CN 1769263	A	20060510	CN 2005-10118852	20011016
TW 251588	B	20060321	TW 2001-90125697	20011017
IN 2003CN00537	A	20050415	IN 2003-CN537	20030411
US 2004030182	A1	20040212	US 2003-418105	20030418
US 7208622	B2	20070424		
PRIORITY APPLN. INFO.:			JP 2000-317604	A 20001018
			CN 2001-820658	A3 20011016
			WO 2001-JP9069	W 20011016

OTHER SOURCE(S): CASREACT 136:325825
AB A process for producing nateglinide crystals comprises reacting trans-4-isopropylcyclohexylcarbonyl chloride with D-phenylalanine in a mixed solvent consisting of a ketone solvent and water in the presence of an alkali to obtain a reaction mixture containing nateglinide, adding an acid to the reaction mixture to make it acidic, and regulating (a) the temperature to

58° to 72° and (b) and the ketone solvent concentration to > 8 weight% and < 22 weight%, to conduct crystallization Nateglinide is a known antidiabetic.
The process is an industrially advantageous method for crystallizing nateglinide.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 32 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:314895 HCAPLUS
DOCUMENT NUMBER: 136:340997
TITLE: Process for preparation of acylphenylalanines
INVENTOR(S): Sumikawa, Michito; Ohgane, Takao
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002032853	A1	20020425	WO 2001-JP9068	20011016
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 200194264	A	20020429	AU 2001-94264	20011016
CA 2425533	A1	20030410	CA 2001-2425533	20011016
EP 1334962	A1	20030813	EP 2001-974874	20011016
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001014728	A	20031014	BR 2001-14728	20011016
RU 2287520	C2	20061120	RU 2003-111012	20011016
TW 575541	B	20040211	TW 2001-90125695	20011017
IN 2003CN00536	A	20050415	IN 2003-CN536	20030411
US 2004024219	A1	20040205	US 2003-418102	20030418
US 7030268	B2	20060418		
US 2006155143	A1	20060713	US 2005-319177	20051228

PRIORITY APPLN. INFO.: JP 2000-317603 A 20001018
WO 2001-JP9068 W 20011016
US 2003-418102 A1 20030418

OTHER SOURCE(S): CASREACT 136:340997
AB This document discloses a process for preparing easily and simply high-purity acylphenylalanines extremely useful as raw materials of drugs or the like, characterized by reacting an acid chloride with phenylalanine in a mixed solvent consisting of an organic solvent and water under conditions made alkaline
with potassium hydroxide.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

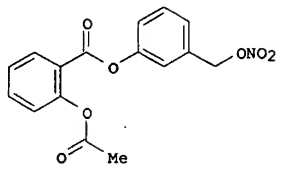
L4 ANSWER 33 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:293592 HCAPLUS
DOCUMENT NUMBER: 136:325420
TITLE: Drugs for diabetes, especially type 2, comprising an antiinflammatory or analgesic drug, selected bivalent linkers, and a nitrate ester
INVENTOR(S): Del Soldato, Piero
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002030867	A2	20020418	WO 2001-EP11665	20011009
WO 2002030867	A3	20020725		
W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IT 2000MI2201	A1	20020412	IT 2000-MI2201	20001012
IT 1319201	B1	20030926		
CA 2425655	A1	20020418	CA 2001-2425655	20011009
AU 200214006	A	20020422	AU 2002-14006	20011009
EP 1324974	A2	20030709	EP 2001-982414	20011009
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004511456	T	20040415	JP 2002-534256	20011009
US 2004023890	A1	20040205	US 2003-398511	20030411

PRIORITY APPLN. INFO.: IT 2000-MI2201 A 20001012
WO 2001-EP11665 W 20011009

OTHER SOURCE(S): MARPAT 136:325420
GI



II

AB Useful for the treatment of diabetes, particularly type 2, are compds. or salts thereof, having the following general formula A-(B)n-(C)m-NO2 [I; wherein A = radical of a drug having an antiinflammatory or analgesic activity; B = bivalent linking group wherein the precursor must meet certain tests described in the application; C = another defined bivalent linking group; n and m = 0 or 1, provided that (n + m) = 1 or 2]. I can be used in conjunction with other antidiabetic drugs, particularly

insulin. I increase the direct antidiabetic effect of insulin, and reduce complications of diabetes, particularly vascular diseases, retinopathies, neuropathies, etc.. The values of n and m, i.e., the presence or absence of bivalent linkers B and C, alone or in combination, are based on performance of the precursors of the linkers in certain tests (no data). These tests are designated as follows: (test 4A): inhibition by > 15% of hemolysis of rat erythrocytes induced by cumene hydroperoxide; (test 5): inhibition of radical production by ≥ 50% in the oxidative degradation of desoxyribose in aqueous Fe2+(NH4)2(SO4)2/thiobarbituric acid solution; and (test 4): inhibition by ≥ 50% of DPPH-induced radical production in MeOH solution For instance, acetylsalicylic acid chloride was esterified with 3-(hydroxymethyl)phenol (80%), followed by nitation of the resultant Ph ester with HNO3/H2SO4 (82%), to give invention compound II, which is thus the 3-(nitrooxymethyl)phenyl ester of aspirin. When tested on isolated aorta from insulin-resistant rats, compound II at a concentration of 10-4 M gave 70% vasorelaxation, relative to non-insulin-resistant controls. This effect was unchanged by the presence or absence of the irreversible NO synthetase inhibitor LNNA. In contrast, both Na nitroprussiate and the indomethacin analog of II, known NO donors, were inactive, and the antidiabetic drug metformin was inactivated by LNNA.

L4 ANSWER 34 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:174779 HCAPLUS
DOCUMENT NUMBER: 137:370326
TITLE: Synthesis of [14C]- and [3H]DJN608 [STARLIX]
AUTHOR(S): Ray, T.; Ciszewska, G.; Wu, A.; Jones, L.
CORPORATE SOURCE: DMPK-Isotope Section, Novartis Pharmaceuticals, E. Hanover, NJ, USA
SOURCE: Synthesis and Applications of Isotopically Labelled Compounds, Proceedings of the International Symposium, 7th, Dresden, Germany, June 18-22, 2000 (2001), Meeting Date 2000, 228-231. Editor(s): Pleiss, Ulrich; Voges, Rolf. John Wiley & Sons Ltd.: Chichester, UK.
CODEN: 69CIJC; ISBN: 0-471-49501-8
DOCUMENT TYPE: Conference
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:370326
AB A novel oral medication for treating type 2 diabetes is trans-N-[[4-(1-methylethyl)cyclohexyl]-carbonyl]-D-phenylalanine, DJN608 [Starlix]. The key step in the synthesis of [14C]DJN608 was the catalytic reduction of [carboxy-14C]cumic acid in the presence of PtO2 at 55 psi of hydrogen in acetic acid to give cis/trans-4-isopropylcyclohexane-[14C]carboxylic acid in 3:1 ratio. Alternatively methods for preparing this mixture of cis- and trans- acids (3:1) are presented. Tritiated DJN608 was prepared by reduction of the corresponding chloro derivative with tritium gas in the presence of 10% palladium on carbon.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

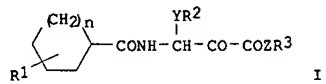
L4 ANSWER 35 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:130037 HCAPLUS
DOCUMENT NUMBER: 137:325603
TITLE: Synthesis of Nateglinide
AUTHOR(S): Zhu, Xue-yan; Peng, Ka; Wang, Xiao-qin; Yang, Li-ping
CORPORATE SOURCE: Dep. Chem., East China Normal Univ., Shanghai, 200062,

Peop. Rep. China
SOURCE: Hecheng Huaxue (2001), 9(6), 537-540
CODEN: HEHUE2; ISSN: 1005-1511
PUBLISHER: Hecheng Huaxue Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
OTHER SOURCE(S): CASREACT 137:325603
AB Title compound, a new antidiabetes medicine, was synthesized from iso-propylbenzene in seven steps, giving the product with overall yield 22%.

L4 ANSWER 36 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:38482 HCAPLUS
DOCUMENT NUMBER: 134:100592
TITLE: Preparation and effect of cycloalkylcarboxamide derivatives as cysteine protease inhibitors
INVENTOR(S): Sato, Masaaki; Mukoyama, Harunobu; Kobayashi, Junichi; Tsuyuki, Shogo; Tokutake, Katsunori; Akabane, Satoshi
PATENT ASSIGNEE(S): Kissei Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 27 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001011037	A	20010116	JP 1999-188275	19990701
PRIORITY APPLN. INFO.:			JP 1999-188275	19990701

OTHER SOURCE(S): MARPAT 134:100592
GI



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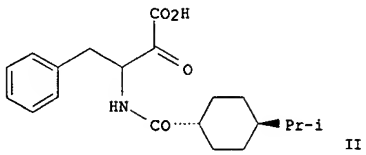
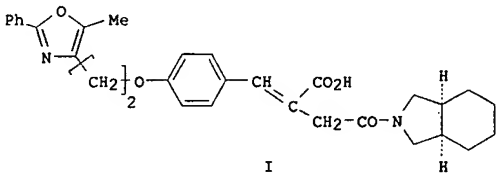


II

AB Title compds. [I; R1 = alkyl; Y = alkylene; R2 = OH, aryl, aryl alkoxy; R3 = H, alkyl, aryl, pyridyl, arylalkyl, pyridylalkyl; Z = O, NH; n = integer 1-3] and stereoisomers are prepared and possesses the cysteine protease inhibitory effect. Title compds. are useful in prevention of arthritis, Alzheimer's disease, rheumatism and osteoporosis. Thus, the title compound II was prepared and tested.

L4 ANSWER 37 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:840649 HCAPLUS
DOCUMENT NUMBER: 134:110109
TITLE: Hybridization of non-sulfonylurea insulin secretagogue and thiazolidinedione-derived insulin sensitizer
AUTHOR(S): Kitajima, Hiroshi; Nakamura, Mitsuharu; Tamakawa, Hiroki; Goto, Nobuharu
CORPORATE SOURCE: Department of Discovery Research, Welfide Corporation, Hirakata, 573-1153, Japan
SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(21), 2453-2456
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Hybrid compds. of non-sulfonylurea insulinotropic agents and thiazolidinedione-derived insulin-sensitizing agents were designed and synthesized. The benzylidenesuccinic acid derivative I was equal both to nateglinide in potency of insulin-releasing activity and to pioglitazone in insulin-sensitizing activity.
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 38 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:228845 HCAPLUS
DOCUMENT NUMBER: 126:220267
TITLE: Structure determination of metabolites isolated form urine and bile after administration of AY4166, a novel D-phenylalanine-derivative hypoglycemic agent. [Erratum to document cited in CA126:325]
AUTHOR(S): Takesada, Hiroko; Matsuda, Keizo; Ohtake, Ryoko; Mihara, Ryuichi; Ono, Ichiro; Tanaka, Kenzo; Naito, Masaki; Yatagai, Masanobu; Suzuki, Ei-Ichiro
CORPORATE SOURCE: Central Research Laboratories, Ajinomoto Co., Inc., Kawasaki, 210, Japan
SOURCE: Bioorganic & Medicinal Chemistry (1997), 5(3), 637

CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB On page 1771 (column 2, line 26) and 1772 (column 1, line 2), the functional group of M2 in Figure 1, which was converted from one of two methyl groups of AY4166, should read hydroxylmethyl instead of methoxyl. On page 1776, column 2, in the parentheses of the fourth line from last, 60 mg/kg should read 60 mg/man.

L4 ANSWER 39 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:702133 HCAPLUS
DOCUMENT NUMBER: 126:325
TITLE: Structure determination of metabolites isolated from urine and bile after administration of AY4166, a novel D-phenylalanine-derivative hypoglycemic agent
AUTHOR(S): Takesada, Hiroko; Matsuda, Keizo; Ohtake, Ryoko; Mihara, Ryuichi; Ono, Ichiro; Tanaka, Kenzo; Naito, Masaki; Yatagai, Masanobu; Suzuki, Ei-ichiro
CORPORATE SOURCE: Central Research Laboratories, Ajinomoto Co., Inc., Kawasaki, 210, Japan
SOURCE: Bioorganic & Medicinal Chemistry (1996), 4(10), 1771-1781
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Mol. structures of 10 metabolites, which were isolated from urine (M1-M8) or bile (M9 and M10) after administration of AY4166 (N-(trans-4-isopropylcyclohexanecarbonyl)-D-phenylalanine), with hypoglycemic activity, were elucidated by mass spectrometry and NMR. Four of these (M1, M2, M3 and M8) were hydroxyl derivs. of AY4166, 2 (M9 and M10) were carboxylate derivs. via oxidation of M2 and M3, 3 (M4, M5 and M6) were glucuronic acid conjugates and the other (M7) was a dehydro derivative The structures for M1, M2, M3, M7, M8, M9 and M10 were confirmed by the coincidence of the retention time of HPLC, MS and 1H-NMR spectra between the isolated metabolites and authentic synthesized substances. For 3 glucuronic acid conjugates, M4, M5 and M6, structural confirmation was performed by a selective enzymic digestion with β-glucuronidase. M1 and M2/3 were about 5-6 and 3-fold less potent than AY4166, resp., and M7 was almost as potent as AY4166.

L4 ANSWER 40 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:468819 HCAPLUS
DOCUMENT NUMBER: 123:55430
TITLE: Preparation of trans-4-isopropylcyclohexanecarboxylic acid chloride
INVENTOR(S): Matsuzawa, Toshihiro; Irie, Yasuo
PATENT ASSIGNEE(S): Ajinomoto KK, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 3 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 07017899	A	19950120	JP 1993-163426	19930701

PRIORITY APPLN. INFO.: JP 1993-163426 19930701
OTHER SOURCE(S): CASREACT 123:55430
AB The title compound (I), useful as an intermediate for antidiabetic N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine, is prepared by treatment of trans-4-isopropylcyclohexanecarboxylic acid (II) with P chloride. II was treated with PCl5 in 1,2-dichloroethane at 40° for 3 h to give 94% I and 0% the cis-isomer, whereas cis-isomer was detected, when SOCl2 was used instead of PCl5.

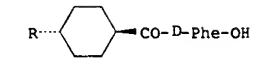
L4 ANSWER 41 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:261002 HCAPLUS
DOCUMENT NUMBER: 118:261002
TITLE: Stable crystals of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine
INVENTOR(S): Sumikawa, Michito; Koguchi, Yoshihito; Ohgane, Takao; Irie, Yasuo; Takahashi, Satoji
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 526171	A2	19930203	EP 1992-306895	19920729
EP 526171	A3	19930505		
EP 526171	B1	19970305		
R: AT, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
JP 05208943	A	19930820	JP 1992-202686	19920729
JP 2508949	B2	19960619		
AT 149483	T	19970315	AT 1992-306895	19920729
ES 2100291	T3	19970616	ES 1992-306895	19920729
CA 2114678	A1	19950802	CA 1994-2114678	19940201
CA 2114678	C	19990427		
PRIORITY APPLN. INFO.:			JP 1991-189696 A	19910730
			JP 1991-199453 A	19910808

AB Stable H-type crystals of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (I) are obtained by treating I with a solvent, at >10°. A solution of 5 g I in 20 mL acetone was added to a stirred mixture of 40 mL acetone and 60 mL water, at 25° to precipitate H-type crystals. The crystals have different m.p., IR spectrum and x-ray diffraction patterns from known forms of I and are not converted to other forms when ground.

L4 ANSWER 42 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1989:458305 HCAPLUS
DOCUMENT NUMBER: 111:58305
TITLE: N-(Cyclohexylcarbonyl)-D-phenylalanines and related compounds. A new class of oral hypoglycemic agents. 2
AUTHOR(S): Shinkai, Hisashi; Nishikawa, Masahiko; Sato, Yusuke; Toi, Koji; Kumashiro, Izumi; Seto, Yoshiko; Fukuma, Mariko; Dan, Katsuaki; Toyoshima, Shigeshi
CORPORATE SOURCE: Cent. Res. Lab., Ajinomoto Co., Inc., Kawasaki, 210, Japan
SOURCE: Journal of Medicinal Chemistry (1989), 32(7), 1436-41
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 111:58305
GI



I

AB A series of analogs, e.g., I (R = alkyl, Ph), of N-(cyclohexylcarbonyl)-D-phenylalanine have been synthesized and evaluated for their hypoglycemic activity. Relationships were studied between the activity and the three-dimensional structure of the acyl moiety, which was characterized by high-resolution 1H NMR spectroscopy and MNDO calcns. The role of the carboxyl group of the phenylalanine moiety was also studied by comparing the activities of the enantiomers, the decarboxyl derivative, the esters, and the amides of the phenylalanine derivs. Thus, the structural requirements for possessing hypoglycemic activity was elucidated and a highly active compound, N-[(trans-4-isopropylcyclohexyl)carbonyl]-D-phenylalanine (I, R = CHMe2) was obtained, which showed a 20% blood glucose decrease at an oral dose of 1.6 mg/kg in fasted normal mice.

L4 ANSWER 43 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1987:85057 HCAPLUS
Correction of: 1987:19047
DOCUMENT NUMBER: 106:85057
Correction of: 106:19047
TITLE: Preparation of D-phenylalanine derivatives and their use as hypoglycemic agents
INVENTOR(S): Toyoshima, Shigeshi; Seto, Yoshiko; Shinkai, Hisashi; Toi, Koji; Kumashiro, Izumi
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: Eur. Pat. Appl., 25 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 196222	A2	19861001	EP 1986-302217	19860326
EP 196222	A3	19880224		
EP 196222	B1	19920129		
R: CH, DE, FR, GB, LI				
JP 63054321	A	19880308	JP 1986-61833	19860319
JP 04015221	B	19920317		
US 4816484	A	19890328	US 1988-146719	19880121
US 34878	E	19950314	US 1993-157564	19931123
PRIORITY APPLN. INFO.:			JP 1985-62276 A	19850327
			JP 1986-38111 A1	19860222
			US 1986-844970 A3	19860327
			US 1988-146719 A5	19880121
			US 1989-844970 B3	19890327

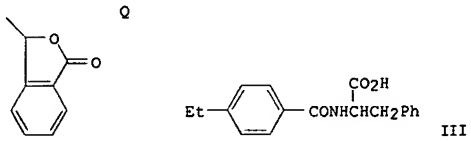
OTHER SOURCE(S): CASREACT 106:85057; MARPAT 106:85057
AB D-Phenylalanine derivs. D-R2CONR3CH(CO2R1)CH2Ph [I; R1 = H, C1-5 alkyl,

C6-12 aryl or aralkyl, Q, CH2CO2R3, CHMeOCOR3, CH2OCOCMe3; R2 = (un)substituted C6-12 aryl, 5- or 6-membered heterocyclyl, cycloalkyl, cycloalkenyl; R3 = H, C1-5 alkyl], their salts. and precursors which can be converted thereto in the human or animal body, useful as hypoglycemics, were prepared via conventional N-acylating reactions. D-Phenylalanine in 10% aqueous NaOH was successively treated with Me2CO, 4-EtC6H4COCl in Me2CO, and 10% aqueous NaOH to give 83% acylphenylanine D-II. At 25 mg/kg in mice, D-II decreased blood glucose 34% in min.

L4 ANSWER 44 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1987:19047 HCAPLUS
DOCUMENT NUMBER: 106:19047
TITLE: Preparation of D-phenylalanine derivatives and their use as hypoglycemic agents
INVENTOR(S): Toyoshima, Shigeshi; Seto, Yoshiko; Shinkai, Hisashi; Toi, Koji; Kumashiro, Izumi
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: Eur. Pat. Appl., 25 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 196222 A2		19861001	EP 1986-302217	19860326
R: CH, DE, FR, GB, LI				
PRIORITY APPLN. INFO.:			JP 1985-62276	19850327

GI



III

AB D-Phenylalanine derivs. D-R2CONR3CH(CO2R1)CH2Ph [I; R1 = H, C1-5 alkyl, C6-12 aryl or aralkyl, Q, CH2CO2R3, CHMeOCOR3, CH2OCOCMe3; R2 = (un)substituted C6-12 aryl, 5- or 6-membered heterocyclyl, cycloalkyl, cycloalkenyl; R3 = H, C1-5 alkyl], their salts, and precursors which can be converted thereto in the human or animal body, useful as hypoglycemics, were prepared via conventional N-acylating reactions. D-Phenylalanine in 10% aqueous NaOH was successively treated with Me2CO, 4-EtC6H4COCl in Me2CO, and 10% aqueous NaOH to give 83% acylphenylanine D-II. At 25 mg/kg in mice, D-II decreased blood glucose 34% in 60 min.

=> fil stng

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	129.72	412.49

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL

	ENTRY	SESSION
CA SUBSCRIBER PRICE	-34.32	-46.02

FILE 'STNGUIDE' ENTERED AT 18:08:42 ON 02 MAY 2007
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
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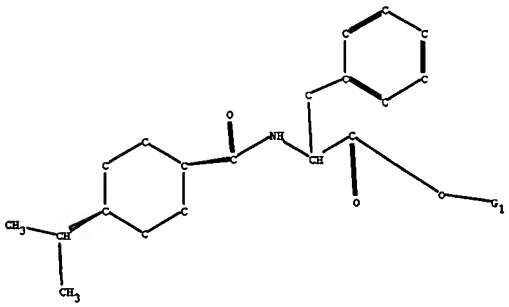
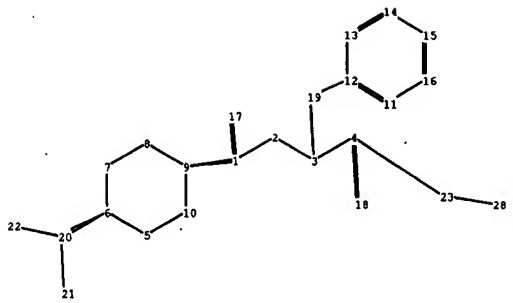
FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Apr 27, 2007 (20070427/UP).

C:\Program Files\Stnexp\Queries\2007 cases\10507255\nateglinide salt.str





chain nodes :
1 2 3 4 17 18 19 20 21 22 23 28
ring nodes :
5 6 7 8 9 10 11 12 13 14 15 16
chain bonds :
1-2 1-9 1-17 2-3 3-4 3-19 4-18 4-23 6-20 12-19 20-21 20-22 23-28
ring bonds :
5-6 5-10 6-7 7-8 8-9 9-10 11-12 11-16 12-13 13-14 14-15 15-16
exact/norm bonds :
1-2 1-17 2-3 4-18 4-23 5-6 5-10 6-7 7-8 8-9 9-10 23-28
exact bonds :
1-9 3-4 3-19 6-20 12-19 20-21 20-22
normalized bonds :
11-12 11-16 12-13 13-14 14-15 15-16

G1:A,H,Ca,K,Mg,Na

Match level :
1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:CLASS 18:CLASS 19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:CLASS 28:CLASS

Stereo Bonds:

9-1 (Single Wedge).
20-6 (Single Hash).

Stereo Chiral Centers:

6 (Parity=Even)
9 (Parity=Odd)

Stereo RSS Sets:

Type=Relative (Default). 2 Nodes= 6 9

```
=> fil reg
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                   ENTRY     SESSION
FULL ESTIMATED COST                                 0.21       0.21

FILE 'REGISTRY' ENTERED AT 18:29:05 ON 02 MAY 2007
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:    1 MAY 2007  HIGHEST RN 934050-43-8
DICTIONARY FILE UPDATES:   1 MAY 2007  HIGHEST RN 934050-43-8

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\2007 cases\10507255\nateglinide salt.str

L1      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1              STR
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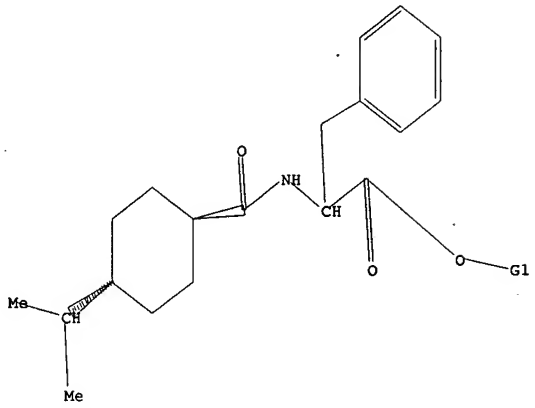

G1 A,H,Ca,K,Mg,Na

Structure attributes must be viewed using STN Express query preparation.

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=> s l1 sss sam
SAMPLE SEARCH INITIATED 18:29:42 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      603 TO ITERATE

100.0% PROCESSED      603 ITERATIONS                              5 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:       10587 TO    13533
PROJECTED ANSWERS:              5 TO      234

L2            5 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 18:29:47 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    11826 TO ITERATE

100.0% PROCESSED    11826 ITERATIONS                            101 ANSWERS
SEARCH TIME: 00.00.01

L3          101 SEA SSS FUL L1

=> fil hcaplu
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                   ENTRY     SESSION
FULL ESTIMATED COST                               172.10     172.31

FILE 'HCAPLUS' ENTERED AT 18:29:57 ON 02 MAY 2007
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FILE COVERS 1907 - 2 May 2007 VOL 146 ISS 19
FILE LAST UPDATED: 1 May 2007 (20070501/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

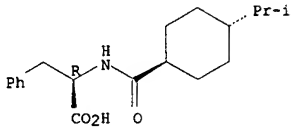
This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3/p
L4 46 L3/P

=> d l4 1-46 hitstr

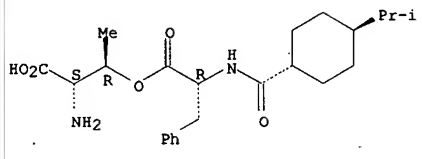
L4 ANSWER 1 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 105816-04-4P, Nateglinide
RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(H type crystal; preparation of H type nateglinide crystal)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



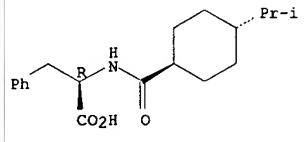
L4 ANSWER 2 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 917394-14-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of L-threonine derivs. with high therapeutic index)
RN 917394-14-0 HCAPLUS
CN L-Threonine, O-[N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-D-phenylalanyl]- (CA INDEX NAME)

Absolute stereochemistry.



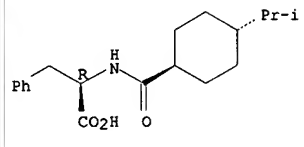
L4 ANSWER 3 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 105816-04-4P, Nateglinide
RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(process for preparation of nateglinide, preferably in B-form)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



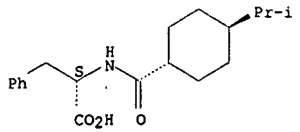
L4 ANSWER 4 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 105816-04-4P, Nateglinide 105816-05-5P, L-Nateglinide
RL: PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(direct separation and enantiosepn. of nateglinide stereoisomers by HPLC)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



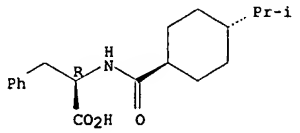
RN 105816-05-5 HCAPLUS
CN L-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



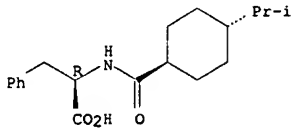
L4 ANSWER 5 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 594837-85-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(in a one-pot process for the preparation of nateglinide)
RN 594837-85-1 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, monosodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 105816-04-4P, Nateglinide
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(one-pot process for the preparation of nateglinide)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

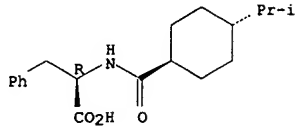
Absolute stereochemistry.



L4 ANSWER 6 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 105816-04-4P, Nateglinide
RL: PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

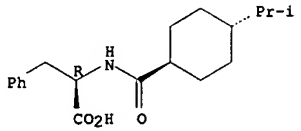
(crystallization of nateglinide as form B)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



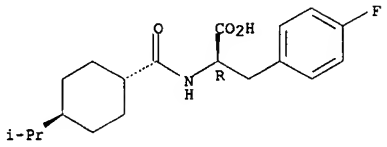
L4 ANSWER 7 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 594837-89-5P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for the preparation of polymorphic crystalline forms of nateglinide ammonium salt)
RN 594837-89-5 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, ammonium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 8 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 909102-82-5P 909102-83-6P 909102-84-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of fluoro-N-[[(isopropyl)cyclohexyl]carbonyl]-D-phenylalanine derivs. (nateglinide analogs) and study of their activity as hypoglycemic agents)
RN 909102-82-5 HCAPLUS
CN D-Phenylalanine, 4-fluoro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, hydrochloride (9CI) (CA INDEX NAME)

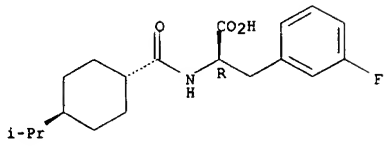
Absolute stereochemistry. Rotation (-).



● HCl

RN 909102-83-6 HCAPLUS
CN D-Phenylalanine, 3-fluoro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, hydrochloride (9CI) (CA INDEX NAME)

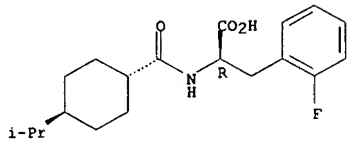
Absolute stereochemistry. Rotation (-).



● HCl

RN 909102-84-7 HCAPLUS
CN D-Phenylalanine, 2-fluoro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



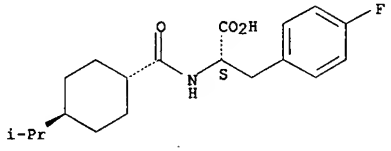
● HCl

IT 909102-79-0P, 4-Fluoro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-L-phenylalanine monohydrochloride 909102-80-3P 909102-81-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation of fluoro-N-[[(isopropyl)cyclohexyl]carbonyl]-L-phenylalanine derivs. (nateglinide analogs) and study of their activity as hypoglycemic agents)

RN 909102-79-0 HCAPLUS
CN L-Phenylalanine, 4-fluoro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, hydrochloride (9CI) (CA INDEX NAME)

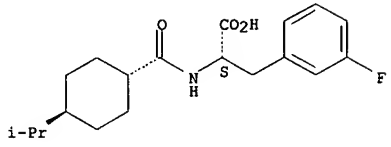
Absolute stereochemistry. Rotation (+).



● HCl

RN 909102-80-3 HCAPLUS
CN L-Phenylalanine, 3-fluoro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, hydrochloride (9CI) (CA INDEX NAME)

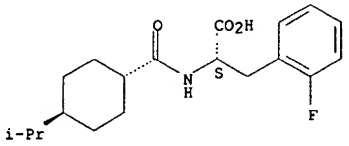
Absolute stereochemistry. Rotation (+).



● HCl

RN 909102-81-4 HCAPLUS
CN L-Phenylalanine, 2-fluoro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, hydrochloride (9CI) (CA INDEX NAME)

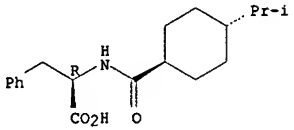
Absolute stereochemistry. Rotation (+).



● HCl

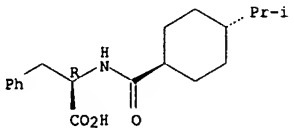
L4 ANSWER 9 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 105816-04-4P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of nateglinide via acylation of phenylalanine with isopropylcyclohexanecarbonyl chloride in a mixture of dioxane or THF and H2O)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



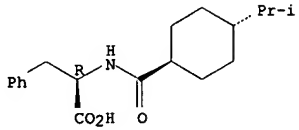
L4 ANSWER 10 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 105816-04-4P, Nateglinide
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of nateglinide via acylation of phenylalanine with isopropylcyclohexanecarbonyl chloride in a mixture of DMF and H2O)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



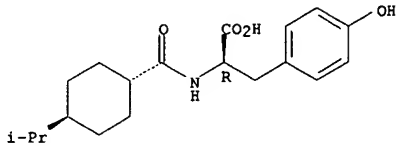
L4 ANSWER 11 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 105816-04-4P, Nateglinide
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(process for the preparation of the crystalline B-form nateglinide from D-phenylalanine Me ester)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



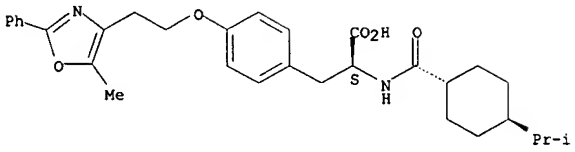
L4 ANSWER 12 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 183996-89-6P 727985-68-4P 727985-69-5P
727985-70-8P 727985-71-9P 727985-72-0P
727985-73-1P 727985-74-2P 727985-75-3P
727985-76-4P 727985-77-5P 727985-78-6P
727985-79-7P 727985-80-0P 727985-81-1P
727985-82-2P 727985-83-3P 727985-84-4P
727985-85-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of alanine derivs. as antidiabetics)
RN 183996-89-6 HCAPLUS
CN D-Tyrosine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



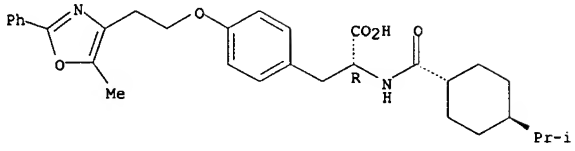
RN 727985-68-4 HCAPLUS
CN L-Tyrosine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-O-[2-(5-methyl-2-phenyl-4-oxazolyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



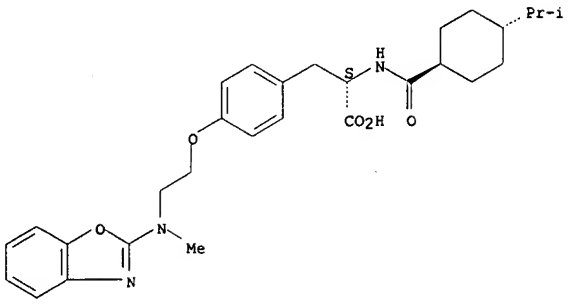
RN 727985-69-5 HCAPLUS
CN D-Tyrosine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-O-[2-(5-methyl-2-phenyl-4-oxazolyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



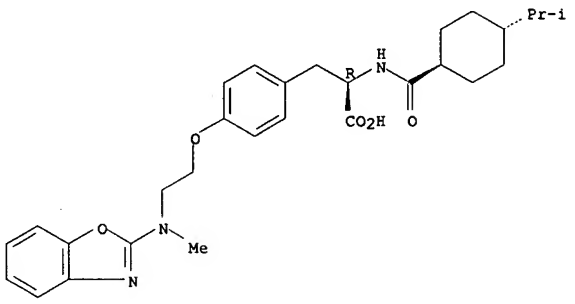
RN 727985-70-8 HCAPLUS
CN L-Tyrosine, O-[2-(2-benzoxazolylmethylamino)ethyl]-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



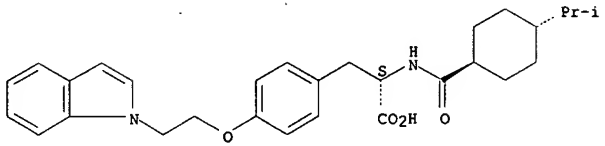
RN 727985-71-9 HCAPLUS
CN D-Tyrosine, O-[2-(2-benzoxazolylmethylamino)ethyl]-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



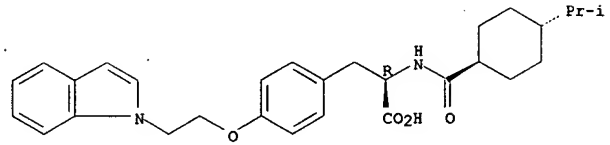
RN 727985-72-0 HCAPLUS
CN L-Tyrosine, O-[2-(1H-indol-1-yl)ethyl]-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



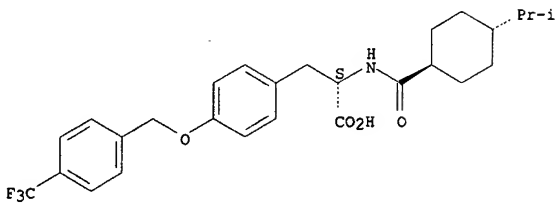
RN 727985-73-1 HCAPLUS
CN D-Tyrosine, O-[2-(1H-indol-1-yl)ethyl]-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



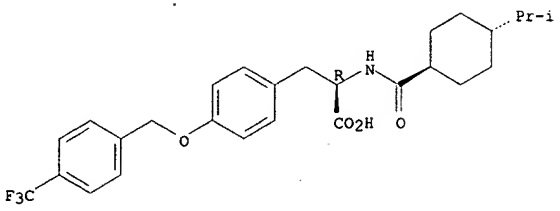
RN 727985-74-2 HCAPLUS
CN L-Tyrosine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-O-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



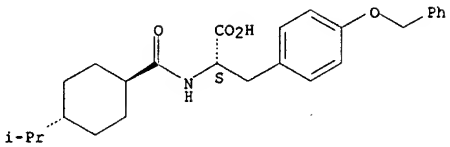
RN 727985-75-3 HCAPLUS
CN D-Tyrosine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-O-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



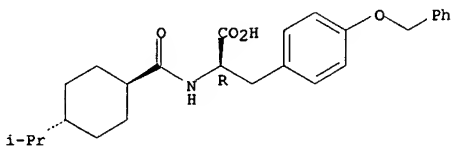
RN 727985-76-4 HCAPLUS
CN L-Tyrosine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-O-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



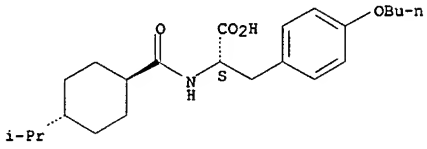
RN 727985-77-5 HCAPLUS
CN D-Tyrosine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-O-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



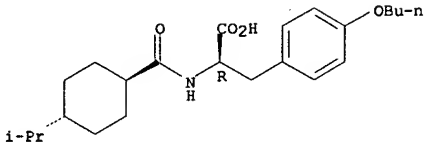
RN 727985-78-6 HCAPLUS
CN L-Tyrosine, O-butyl-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



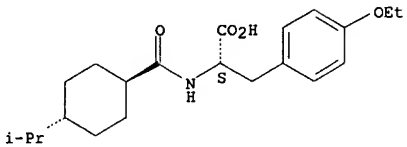
RN 727985-79-7 HCAPLUS
CN D-Tyrosine, O-butyl-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 727985-80-0 HCAPLUS
CN L-Tyrosine, O-ethyl-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

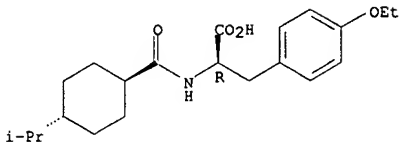
Absolute stereochemistry. Rotation (+).



RN 727985-81-1 HCAPLUS

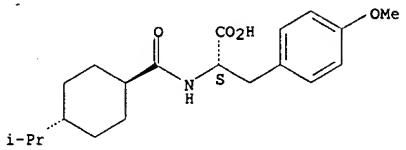
CN D-Tyrosine, O-ethyl-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



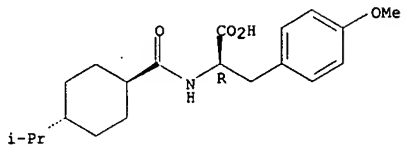
RN 727985-82-2 HCAPLUS
CN L-Tyrosine, O-methyl-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



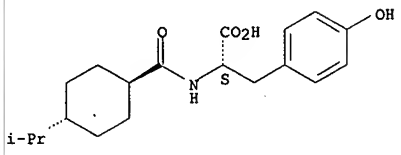
RN 727985-83-3 HCAPLUS
CN D-Tyrosine, O-methyl-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



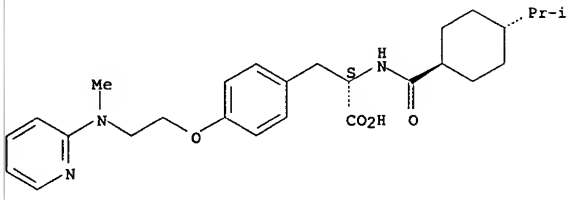
RN 727985-84-4 HCAPLUS
CN L-Tyrosine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



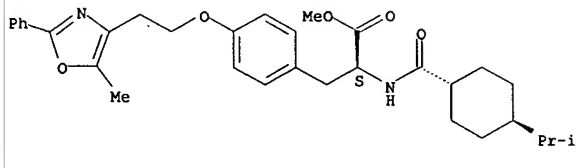
RN 727985-85-5 HCAPLUS
CN L-Tyrosine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-O-[2-(methyl-2-pyridinylamino)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



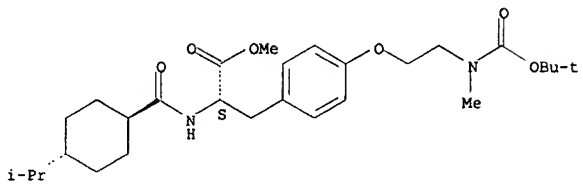
IT 727985-89-9P 727985-92-4P 727985-93-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of alanine derivs. as antidiabetics)
RN 727985-89-9 HCAPLUS
CN L-Tyrosine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-O-[2-(5-methyl-2-phenyl-4-oxazolyl)ethyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



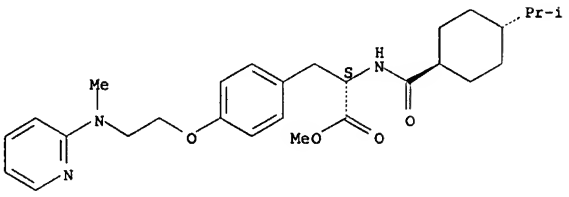
RN 727985-92-4 HCAPLUS
CN L-Tyrosine, O-[2-[[(1,1-dimethylethoxy)carbonyl]methylamino]ethyl]-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



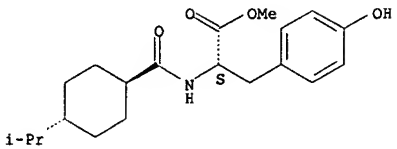
RN 727985-93-5 HCAPLUS
CN L-Tyrosine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-O-[2-(methyl-2-pyridinylamino)ethyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



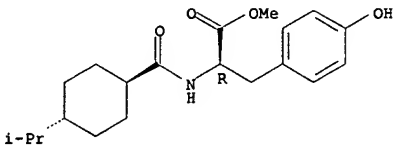
IT 727985-87-7P 727985-88-8P
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of alanine derivs. as antidiabetics)
RN 727985-87-7 HCAPLUS
CN L-Tyrosine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



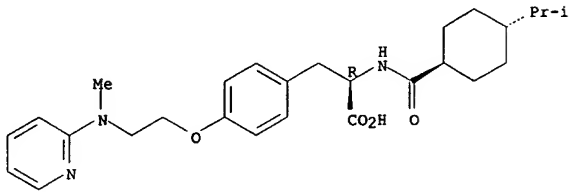
RN 727985-88-8 HCAPLUS
CN D-Tyrosine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



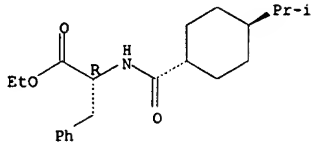
IT 727985-86-6P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of alanine derivs. as antidiabetics)
RN 727985-86-6 HCAPLUS
CN D-Tyrosine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-O-[2-(methyl-2-pyridinylamino)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L4 ANSWER 13 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 187728-85-4P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(targeted pancreatic β-cell imaging and therapy)
RN 187728-85-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

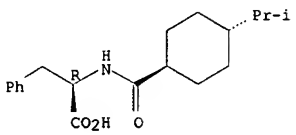


L4 ANSWER 14 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 105816-04-4DP, Nateglinide, analogs 851863-95-1P
851863-97-3P 851863-99-5P 851864-01-2P

851864-03-4P 851864-05-6P 851864-07-8P
851864-09-0P 851864-11-4P 851864-13-6P
851864-15-8P 851864-17-0P 851864-19-2P
851864-21-6P 851864-23-8P 851864-25-0P
851864-27-2P 851864-29-4P 851864-31-8P
851864-33-0P 851864-35-2P 851864-37-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(syntheses and hypoglycemia activities of N-(trans-4-isopropylcyclohexylcarbonyl)-β-ring substituted phenylalanines)

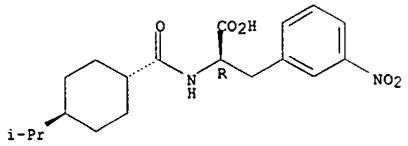
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



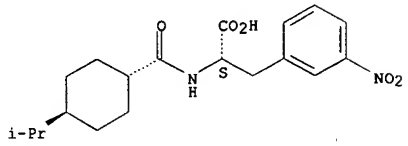
RN 851863-95-1 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-3-nitro- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 851863-97-3 HCAPLUS
CN L-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-3-nitro- (9CI) (CA INDEX NAME)

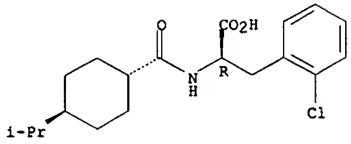
Absolute stereochemistry. Rotation (+).



RN 851863-99-5 HCAPLUS
CN D-Phenylalanine, 2-chloro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-

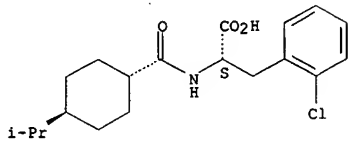
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



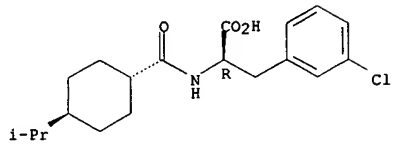
RN 851864-01-2 HCAPLUS
CN L-Phenylalanine, 2-chloro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



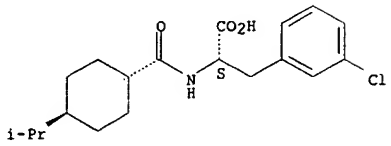
RN 851864-03-4 HCAPLUS
CN D-Phenylalanine, 3-chloro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



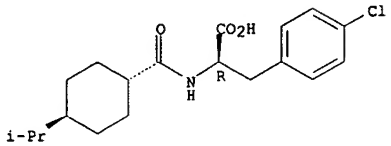
RN 851864-05-6 HCAPLUS
CN L-Phenylalanine, 3-chloro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



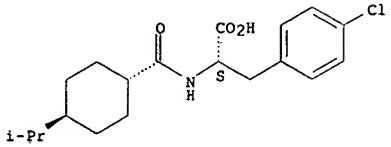
RN 851864-07-8 HCAPLUS
CN D-Phenylalanine, 4-chloro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



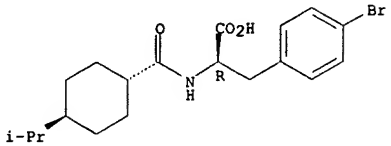
RN 851864-09-0 HCAPLUS
CN L-Phenylalanine, 4-chloro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 851864-11-4 HCAPLUS
CN D-Phenylalanine, 4-bromo-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-
(9CI) (CA INDEX NAME)

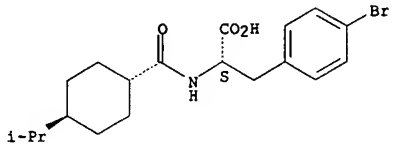
Absolute stereochemistry.



RN 851864-13-6 HCAPLUS

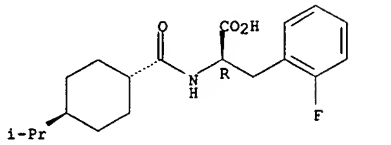
CN L-Phenylalanine, 4-bromo-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



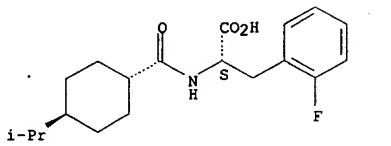
RN 851864-15-8 HCAPLUS
CN D-Phenylalanine, 2-fluoro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



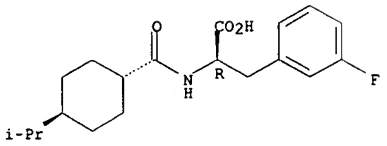
RN 851864-17-0 HCAPLUS
CN L-Phenylalanine, 2-fluoro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



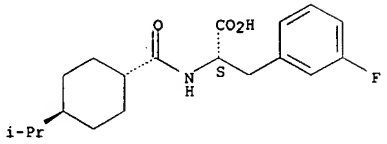
RN 851864-19-2 HCAPLUS
CN D-Phenylalanine, 3-fluoro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



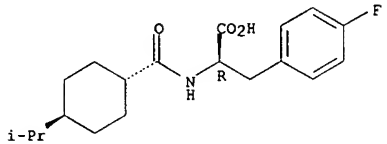
RN 851864-21-6 HCAPLUS
CN L-Phenylalanine, 3-fluoro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



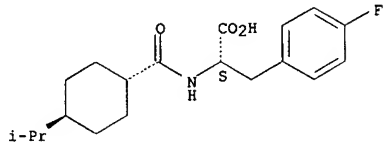
RN 851864-23-8 HCAPLUS
CN D-Phenylalanine, 4-fluoro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 851864-25-0 HCAPLUS
CN L-Phenylalanine, 4-fluoro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

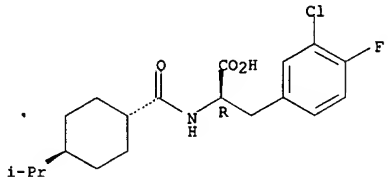
Absolute stereochemistry. Rotation (+).



RN 851864-27-2 HCAPLUS

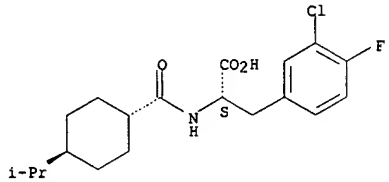
CN D-Phenylalanine, 3-chloro-4-fluoro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



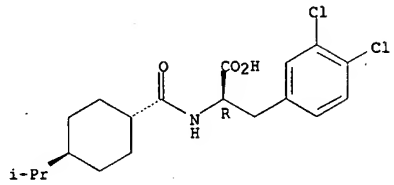
RN 851864-29-4 HCAPLUS
CN L-Phenylalanine, 3-chloro-4-fluoro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



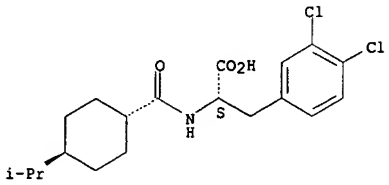
RN 851864-31-8 HCAPLUS
CN D-Phenylalanine, 3,4-dichloro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



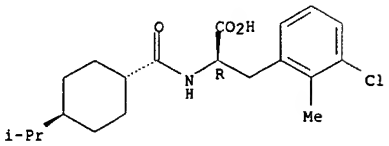
RN 851864-33-0 HCAPLUS
CN L-Phenylalanine, 3,4-dichloro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



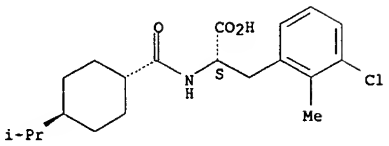
RN 851864-35-2 HCAPLUS
CN D-Phenylalanine, 3-chloro-2-methyl-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 851864-37-4 HCAPLUS
CN L-Phenylalanine, 3-chloro-2-methyl-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

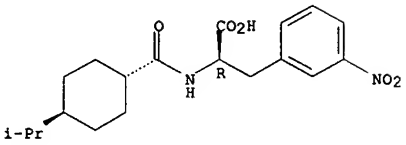
Absolute stereochemistry. Rotation (+).



L4 ANSWER 15 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 851863-95-1P 851863-97-3P 851863-99-5P
851864-01-2P 851864-03-4P 851864-05-6P
851864-07-8P 851864-09-0P 851864-11-4P
851864-13-6P 851864-15-8P 851864-17-0P
851864-19-2P 851864-21-6P 851864-23-8P
851864-25-0P 851864-27-2P 851864-29-4P
851864-31-8P 851864-33-0P 851864-35-2P
851864-37-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aromatic amino acid derivs. for treatment of blood sugar disorders)

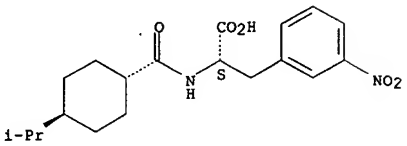
RN 851863-95-1 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-3-nitro- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



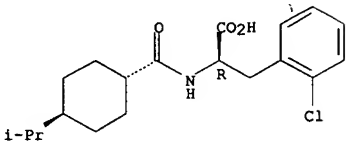
RN 851863-97-3 HCAPLUS
CN L-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-3-nitro- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



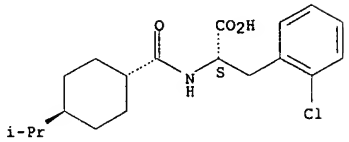
RN 851863-99-5 HCAPLUS
CN D-Phenylalanine, 2-chloro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



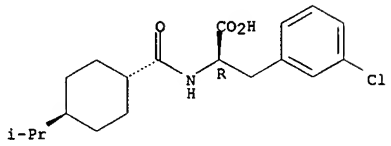
RN 851864-01-2 HCAPLUS
CN L-Phenylalanine, 2-chloro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



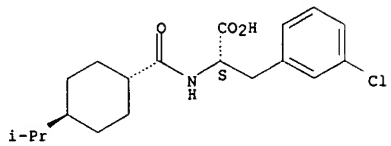
RN 851864-03-4 HCAPLUS
CN D-Phenylalanine, 3-chloro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



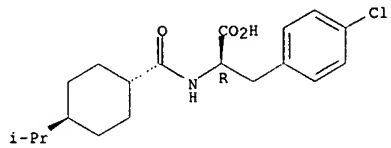
RN 851864-05-6 HCAPLUS
CN L-Phenylalanine, 3-chloro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 851864-07-8 HCAPLUS
CN D-Phenylalanine, 4-chloro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-
(9CI) (CA INDEX NAME)

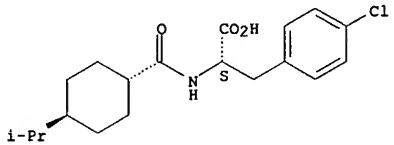
Absolute stereochemistry. Rotation (-).



RN 851864-09-0 HCAPLUS

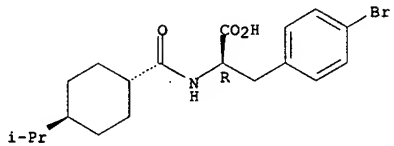
CN L-Phenylalanine, 4-chloro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



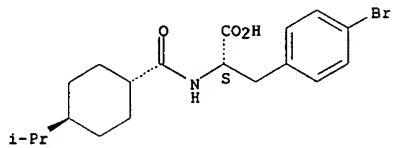
RN 851864-11-4 HCAPLUS
CN D-Phenylalanine, 4-bromo-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



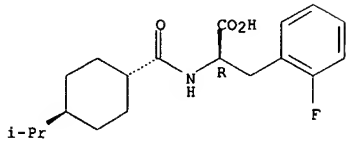
RN 851864-13-6 HCAPLUS
CN L-Phenylalanine, 4-bromo-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



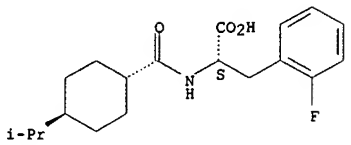
RN 851864-15-8 HCAPLUS
CN D-Phenylalanine, 2-fluoro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



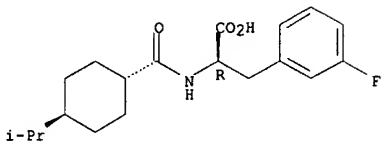
RN 851864-17-0 HCAPLUS
CN L-Phenylalanine, 2-fluoro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



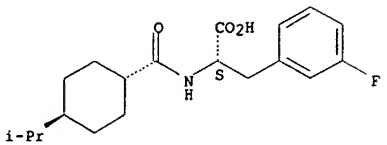
RN 851864-19-2 HCAPLUS
CN D-Phenylalanine, 3-fluoro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 851864-21-6 HCAPLUS
CN L-Phenylalanine, 3-fluoro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-
(9CI) (CA INDEX NAME)

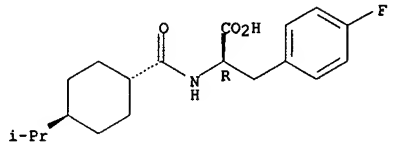
Absolute stereochemistry. Rotation (+).



RN 851864-23-8 HCAPLUS

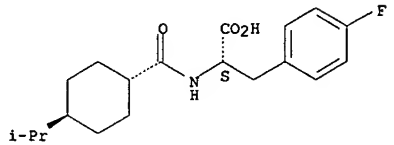
CN D-Phenylalanine, 4-fluoro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



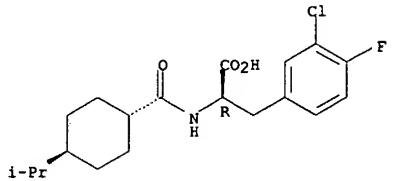
RN 851864-25-0 HCAPLUS
CN L-Phenylalanine, 4-fluoro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



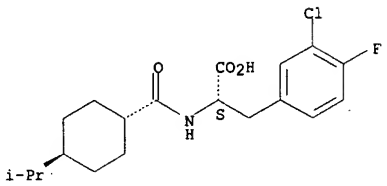
RN 851864-27-2 HCAPLUS
CN D-Phenylalanine, 3-chloro-4-fluoro-N-[[trans-4-(1-
methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



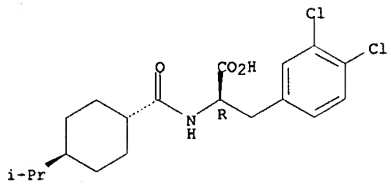
RN 851864-29-4 HCAPLUS
CN L-Phenylalanine, 3-chloro-4-fluoro-N-[[trans-4-(1-
methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



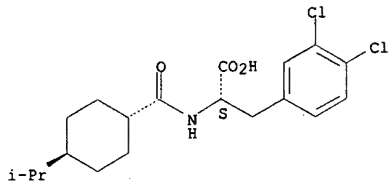
RN 851864-31-8 HCAPLUS
CN D-Phenylalanine, 3,4-dichloro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



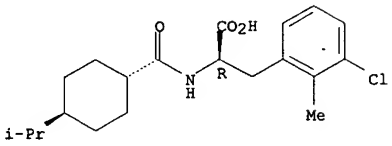
RN 851864-33-0 HCAPLUS
CN L-Phenylalanine, 3,4-dichloro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



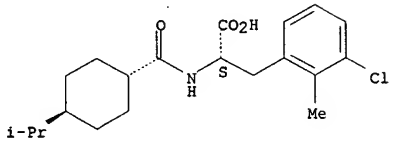
RN 851864-35-2 HCAPLUS
CN D-Phenylalanine, 3-chloro-2-methyl-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



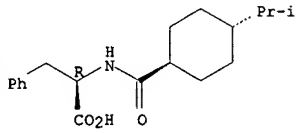
RN 851864-37-4 HCAPLUS
CN L-Phenylalanine, 3-chloro-2-methyl-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



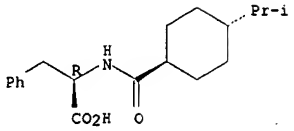
L4 ANSWER 16 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 105816-04-4P, Nateglinide
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(preparation of crystalline form of nateglinide for dosage forms)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



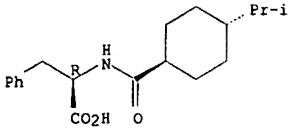
L4 ANSWER 17 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 105816-04-4P, Nateglinide
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(saponification and neutralization process for the preparation of chirally pure
nateglinide from its lower alkyl esters and nateglinide polymorphic crystalline modifications)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



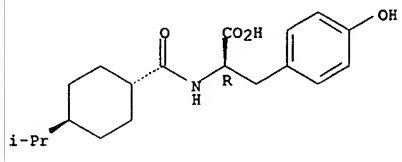
L4 ANSWER 18 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 105816-04-4P, Nateglinide
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(large scale synthesis of nateglinide)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



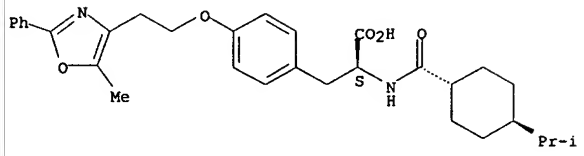
L4 ANSWER 19 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 183996-89-6P 727985-68-4P 727985-69-5P
727985-70-8P 727985-71-9P 727985-72-0P
727985-73-1P 727985-74-2P 727985-75-3P
727985-76-4P 727985-77-5P 727985-78-6P
727985-79-7P 727985-80-0P 727985-81-1P
727985-82-2P 727985-83-3P 727985-84-4P
727985-85-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of alanine compds. as antidiabetics)
RN 183996-89-6 HCAPLUS
CN D-Tyrosine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



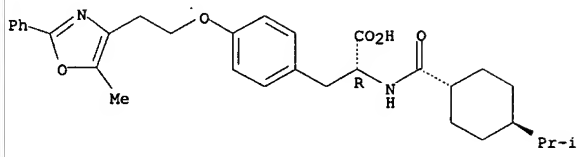
RN 727985-68-4 HCAPLUS
CN L-Tyrosine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-O-[2-(5-methyl-2-phenyl-4-oxazolyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



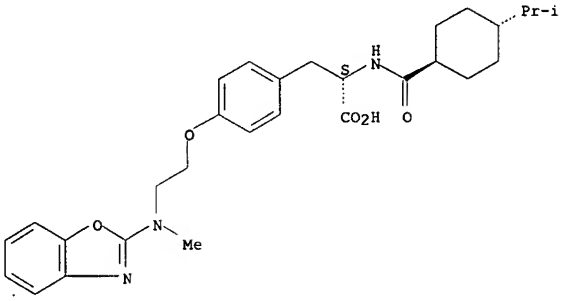
RN 727985-69-5 HCAPLUS
CN D-Tyrosine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-O-[2-(5-methyl-2-phenyl-4-oxazolyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



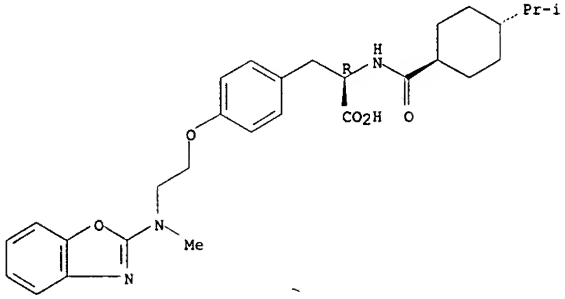
RN 727985-70-8 HCAPLUS
CN L-Tyrosine, O-[2-(2-benzoxazolylmethylamino)ethyl]-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



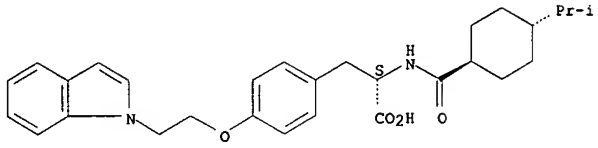
RN 727985-71-9 HCAPLUS
CN D-Tyrosine, O-[2-(2-benzoxazolylmethylamino)ethyl]-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



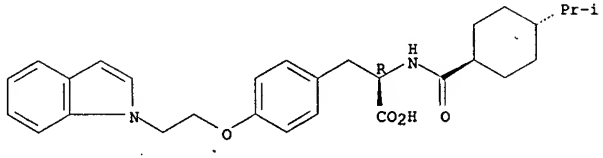
RN 727985-72-0 HCAPLUS
CN L-Tyrosine, O-[2-(1H-indol-1-yl)ethyl]-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



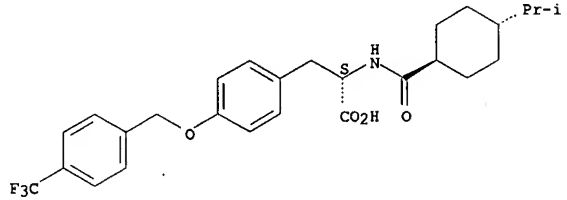
RN 727985-73-1 HCAPLUS
CN D-Tyrosine, O-[2-(1H-indol-1-yl)ethyl]-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



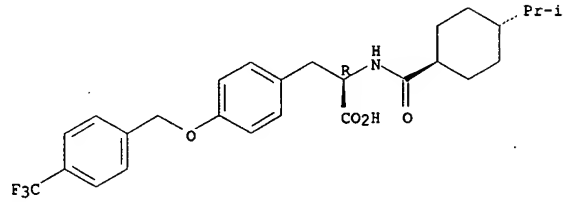
RN 727985-74-2 HCAPLUS
CN L-Tyrosine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-O-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



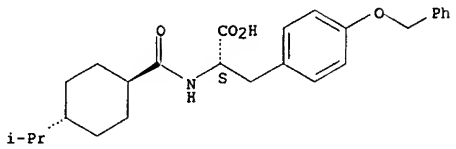
RN 727985-75-3 HCAPLUS
CN D-Tyrosine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-O-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



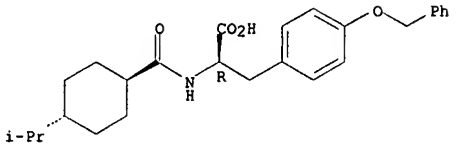
RN 727985-76-4 HCAPLUS
CN L-Tyrosine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-O-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



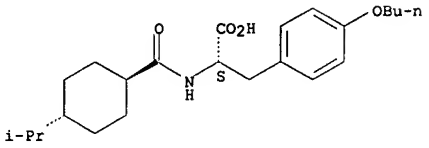
RN 727985-77-5 HCAPLUS
CN D-Tyrosine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-O-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



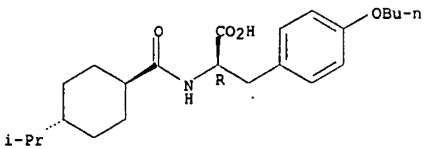
RN 727985-78-6 HCAPLUS
CN L-Tyrosine, O-butyl-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



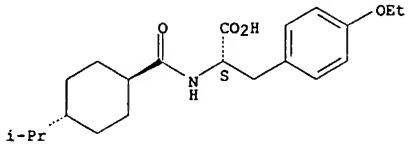
RN 727985-79-7 HCAPLUS
CN D-Tyrosine, O-butyl-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



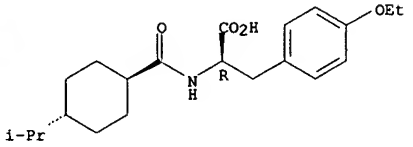
RN 727985-80-0 HCAPLUS
CN L-Tyrosine, O-ethyl-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



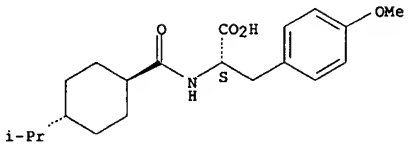
RN 727985-81-1 HCAPLUS
CN D-Tyrosine, O-ethyl-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



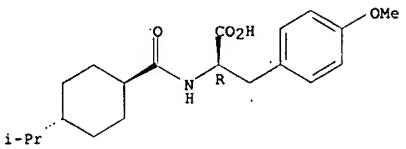
RN 727985-82-2 HCAPLUS
CN L-Tyrosine, O-methyl-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



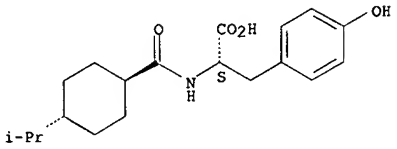
RN 727985-83-3 HCAPLUS
CN D-Tyrosine, O-methyl-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



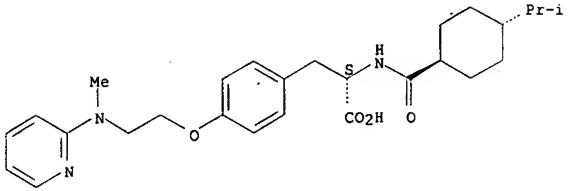
RN 727985-84-4 HCAPLUS
CN L-Tyrosine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



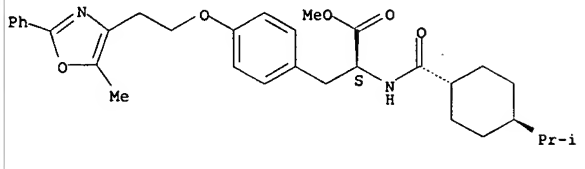
RN 727985-85-5 HCAPLUS
CN L-Tyrosine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-O-[2-(methyl-2-pyridinylamino)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



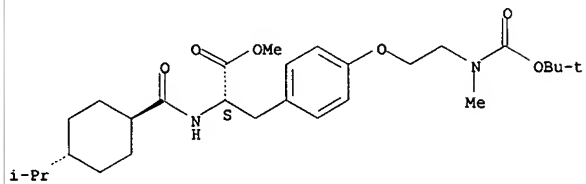
IT 727985-89-9P 727985-92-4P 727985-93-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of alanine compds. as antidiabetics)
RN 727985-89-9 HCAPLUS
CN L-Tyrosine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-O-[2-(5-methyl-2-phenyl-4-oxazolyl)ethyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



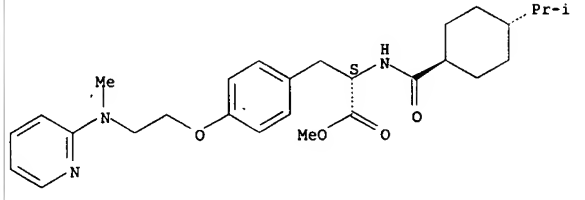
RN 727985-92-4 HCAPLUS
CN L-Tyrosine, O-[2-[[(1,1-dimethylethoxy)carbonyl]methylamino]ethyl]-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



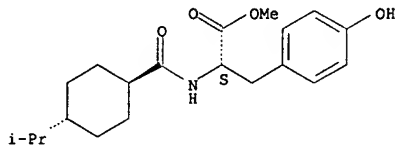
RN 727985-93-5 HCAPLUS
CN L-Tyrosine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-O-[2-(methyl-2-pyridinylamino)ethyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



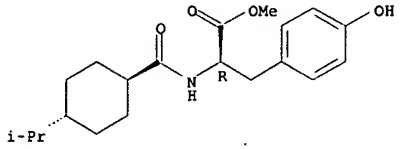
IT 727985-87-7P 727985-88-8P
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of alanine compds. as antidiabetics)
RN 727985-87-7 HCAPLUS
CN L-Tyrosine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



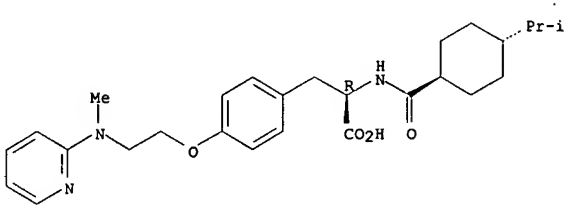
RN 727985-88-8 HCAPLUS
CN D-Tyrosine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



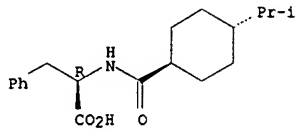
IT 727985-86-6P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of alanine compds. as antidiabetics)
RN 727985-86-6 HCAPLUS
CN D-Tyrosine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-O-[2-(methyl-2-pyridinylamino)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L4 ANSWER 20 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 105816-04-4P, Nateglinide
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(process for the formation of a crystalline polymorphic form of nateglinide)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.

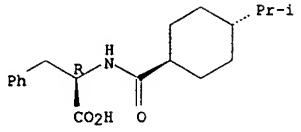


L4 ANSWER 21 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 669087-90-5P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pharmaceutical compns. containing nateglinide inclusion complexes with β-cyclodextrin and its derivs.)
RN 669087-90-5 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with β-cyclodextrin (3:1) (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.



CM 2

CRN 7585-39-9
CMF C42 H70 O35

Absolute stereochemistry.

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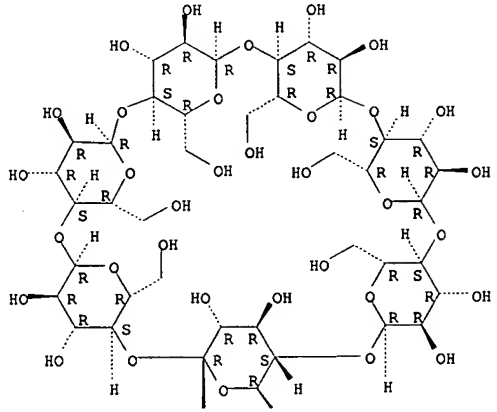

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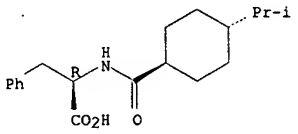
IT 105816-04-4DP, Nateglinide, complexes with hydroxypropyl β-cyclodextrin 669087-91-6P 669087-92-7P 669087-93-8P 669087-94-9P 669087-95-0P 669088-00-0P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pharmaceutical compns. containing nateglinide inclusion complexes with β-cyclodextrin and its derivs.)

RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.

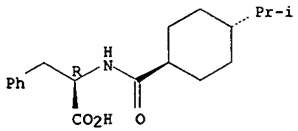


RN 669087-91-6 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with β-cyclodextrin (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.

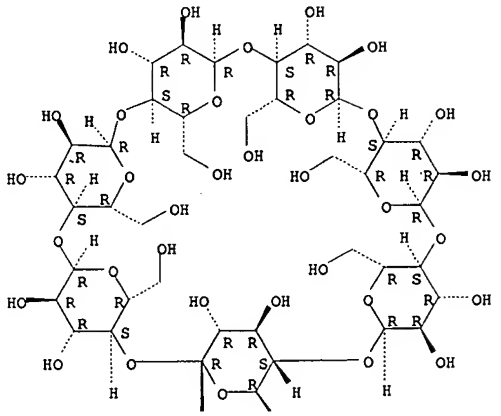


CM 2

CRN 7585-39-9
CMF C42 H70 O35

Absolute stereochemistry.

PAGE 1-A



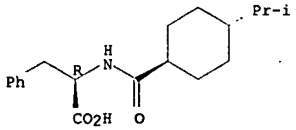
PAGE 2-A

RN 669087-92-7 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with 2A,2B,2C,2D,2E,2F,2G,6A,6B,6C,6D,6E,6F,6G-tetradeca-O-methyl- β-cyclodextrin (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.

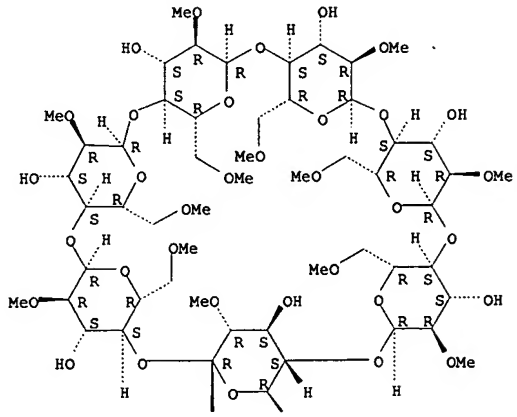


CM 2

CRN 51166-71-3
CMF C56 H98 O35

Absolute stereochemistry.

PAGE 1-A



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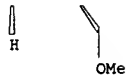
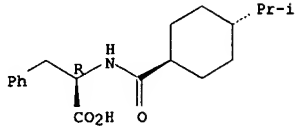


RN 669087-93-8 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with 2A,2B,2C,2D,2E,2F,2G,3A,3B,3C,3D,3E,3F,3G,6A,6B,6C,6D,6E,6F,6G-heneicosa-O-methyl-β-cyclodextrin (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.

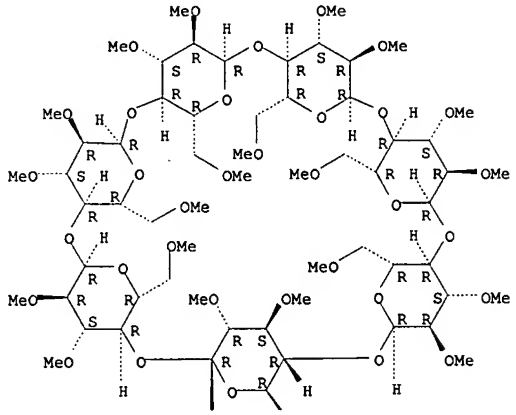


CM 2

CRN 55216-11-0
CMF C63 H112 O35

Absolute stereochemistry.

PAGE 1-A



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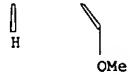


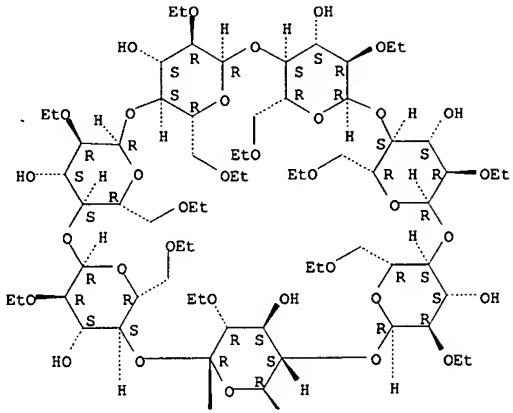
RN 669087-94-9 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with 2A,2B,2C,2D,2E,2F,2G,6A,6B,6C,6D,6E,6F,6G-tetradeca-O-ethyl- β-cyclodextrin (1:1) (9CI) (CA INDEX NAME)

CM 1

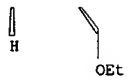
CRN 111689-03-3
CMF C70 H126 O35

Absolute stereochemistry.

PAGE 1-A



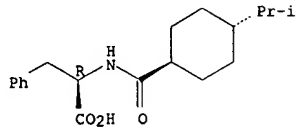
PAGE 2-A



CM 2

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.

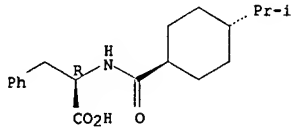


RN 669087-95-0 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with β-cyclodextrin (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.

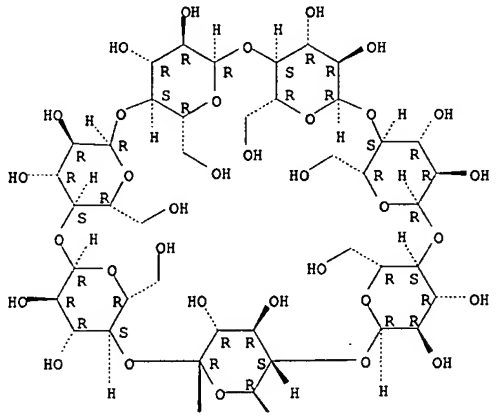


CM 2

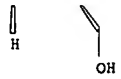
CRN 7585-39-9
CMF C42 H70 O35

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



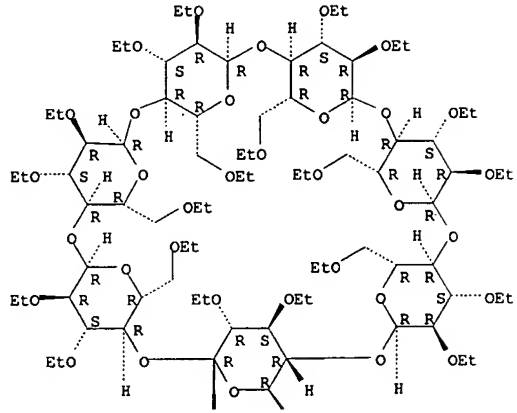
RN 669088-00-0 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with 2A,2B,2C,2D,2E,2F,2G,3A,3B,3C,3D,3E,3F,3G,6A,6B,6C,6D,6E,6F,6G-heneicosa-O-ethyl-β-cyclodextrin (1:1) (9CI) (CA INDEX NAME)

CM 1

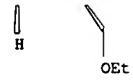
CRN 111689-01-1
CMF C84 H154 O35

Absolute stereochemistry.

PAGE 1-A



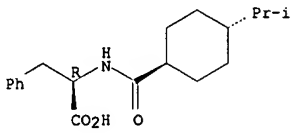
PAGE 2-A



CM 2

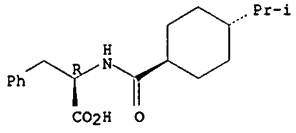
CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.



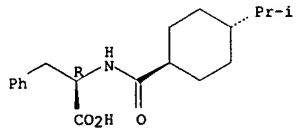
L4 ANSWER 22 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 105816-04-4P, Nateglinide
RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(synthesis and purification of nateglinide)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 23 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 105816-04-4P, Nateglinide
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses)
(preparation of polymorphic forms of nateglinide)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

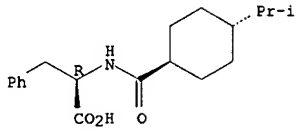
Absolute stereochemistry.



IT 105816-04-4DP, Nateglinide, polymorphs 651353-42-3P
651353-43-4P 651353-44-5P 651353-45-6P
651353-46-7P 651353-47-8P 651353-48-9P
651353-49-0P 651353-50-3P 651353-51-4P
651353-52-5P 651353-53-6P 651353-54-7P
RL: PEP (Physical, engineering or chemical process); PYP (Physical

process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(preparation of polymorphic forms of nateglinide)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.

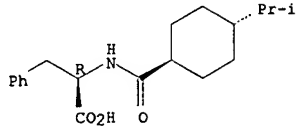


RN 651353-42-3 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with methanol (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.



CM 2

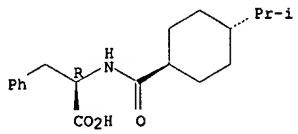
CRN 67-56-1
CMF C H4 O

RN 651353-43-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with ethanol (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.



CM 2

CRN 64-17-5
CMF C2 H6 O

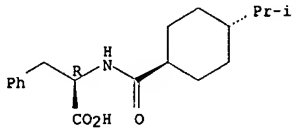
H_3C-CH_2-OH

RN 651353-44-5 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with 1-butanol (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.



CM 2

CRN 71-36-3
CMF C4 H10 O

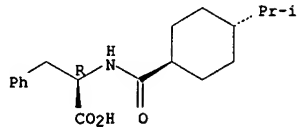
$H_3C-CH_2-CH_2-CH_2-OH$

RN 651353-45-6 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with 1-propanol (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.



CM 2

CRN 71-23-8
CMF C3 H8 O

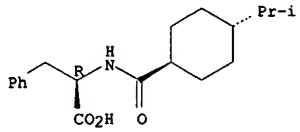
$H_3C-CH_2-CH_2-OH$

RN 651353-46-7 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with N,N-dimethylacetamide (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.



CM 2

CRN 127-19-5
CMF C4 H9 N O

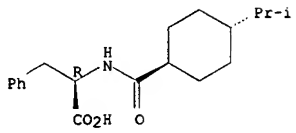
RN 651353-47-8 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with 1-methyl-2-pyrrolidinone (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4

CMF C19 H27 N O3

Absolute stereochemistry.



CM 2

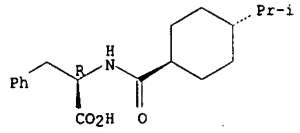
CRN 872-50-4
CMF C5 H9 N O

RN 651353-48-9 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with N,N-dimethylformamide (9CI) (CA INDEX NAME)

CM 1

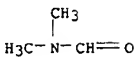
CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.



CM 2

CRN 68-12-2
CMF C3 H7 N O

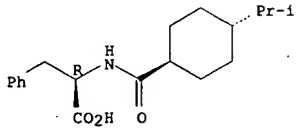


RN 651353-49-0 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with 1,2-dimethoxyethane (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.



CM 2

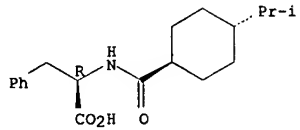
CRN 110-71-4
CMF C4 H10 O2

RN 651353-50-3 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with dimethylbenzene (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.



CM 2

CRN 1330-20-7
CMF C8 H10
CCI IDS

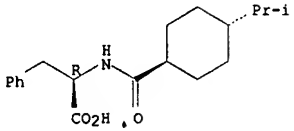
2 (D1-Me)

RN 651353-51-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with tetrachloromethane (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.



CM 2

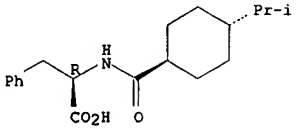
CRN 56-23-5
CMF C Cl4

RN 651353-52-5 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with 1,2-dichloroethane (9CI) (CA INDEX NAME)

CM 1

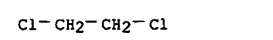
CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.



CM 2

CRN 107-06-2
CMF C2 H4 Cl2

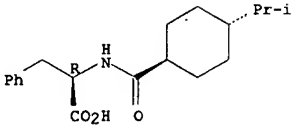


RN 651353-53-6 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with trichloromethane (9CI) (CA INDEX NAME)

CM 1

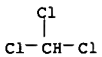
CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.



CM 2

CRN 67-66-3
CMF C H Cl3

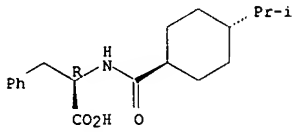


RN 651353-54-7 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with heptane (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.



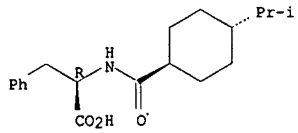
CM 2

CRN 142-82-5
CMF C7 H16

Me— $(CH_2)_5$ — Me

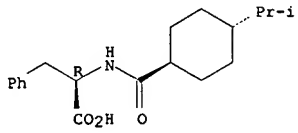
L4 ANSWER 24 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 105816-04-4P, Nateglinide
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for preparation of nateglinide)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



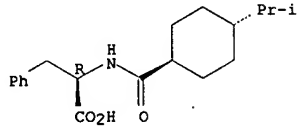
L4 ANSWER 25 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 105816-04-4P, Nateglinide
RL: IMF (Industrial manufacture); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); PREP (Preparation); PROC (Process)
(process for the preparation of a crystal polymorphic form of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (nateglinide))
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 26 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 105816-04-4P, Nateglinide
RL: PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of A, M, and P type nateglinide crystals by crystallization from mixture
of solvents)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.

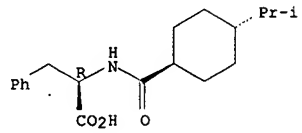


L4 ANSWER 27 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 592523-31-4P 592523-32-5P 592524-24-8P
594837-85-1P 594837-86-2P 594837-87-3P
594837-89-5P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and properties of nateglinide salts)
RN 592523-31-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with 1-deoxy-1-(methylamino)-D-glucitol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

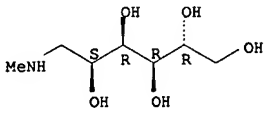
Absolute stereochemistry.



CM 2

CRN 6284-40-8
CMF C7 H17 N O5

Absolute stereochemistry.

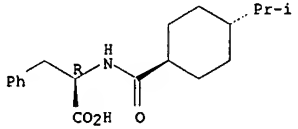


RN 592523-32-5 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with 2-amino-2-(hydroxymethyl)-1,3-propanediol (1:1) (9CI) (CA INDEX NAME)

CM 1

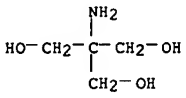
CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.



CM 2

CRN 77-86-1
CMF C4 H11 N O3

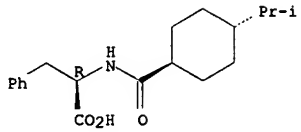


RN 592524-24-8 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with L-lysine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

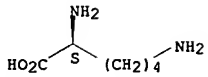
Absolute stereochemistry.



CM 2

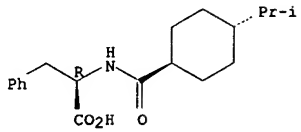
CRN 56-87-1
CMF C6 H14 N2 O2

Absolute stereochemistry.



RN 594837-85-1 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, monosodium salt (9CI) (CA INDEX NAME)

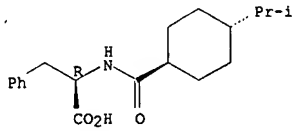
Absolute stereochemistry.



● Na

RN 594837-86-2 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, monopotassium salt (9CI) (CA INDEX NAME)

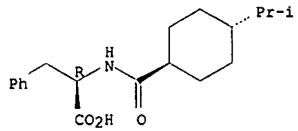
Absolute stereochemistry.



● K

RN 594837-87-3 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, calcium salt (2:1) (9CI) (CA INDEX NAME)

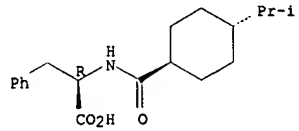
Absolute stereochemistry.



●1/2 Ca

RN 594837-89-5 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, ammonium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

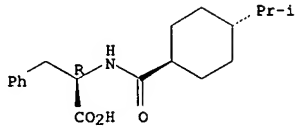


● x NH_3

L4 ANSWER 28 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 105816-04-4P, Nateglinide
RL: PNU (Preparation, unclassified); PREP (Preparation)
(preparation of)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA

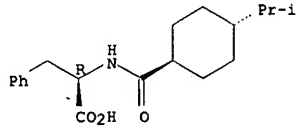
INDEX NAME)

Absolute stereochemistry.



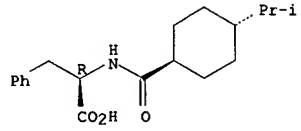
L4 ANSWER 29 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 105816-04-4P, Nateglinide
RL: PNU (Preparation, unclassified); PREP (Preparation)
(synthesis of trans-4-isopropylcyclohexanecarboxylic acid as intermediate for nateglinide)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 30 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 105816-04-4P
RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); ANST (Analytical study); BIOL (Biological study); PREP (Preparation)
(separation of cis-isomer of nateglinide by HPLC method)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

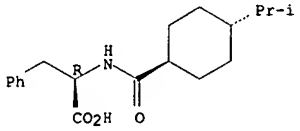
Absolute stereochemistry.



L4 ANSWER 31 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 105816-04-4P, Nateglinide

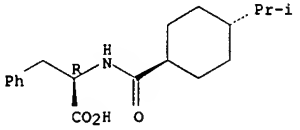
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of nateglinide as antidiabetic drug)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



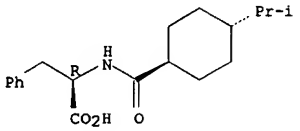
L4 ANSWER 32 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 105816-04-4P, Nateglinide
RL: PAC (Pharmacological activity); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(industrial process for producing B-form nateglinide crystals)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



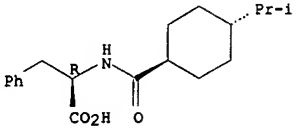
L4 ANSWER 33 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 105816-04-4P, Nateglinide
RL: IMF (Industrial manufacture); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for producing nateglinide crystals)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



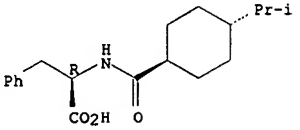
L4 ANSWER 34 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 105816-04-4P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for preparation of acylphenylalanines)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 35 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 105816-04-4DP, Nateglinide, nitroxyl-containing derivs.
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidates; preparation of antidiabetic agents comprising antiinflammatory or analgesic drugs, selected bivalent linkers, and nitrate esters)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

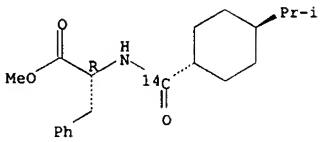
Absolute stereochemistry.



L4 ANSWER 36 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 475168-20-8P 475168-27-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

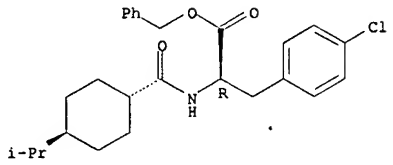
(stereoselective preparation of [14C]- and [3H]DJN608 [Starlix])
RN 475168-20-8 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl-14C]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



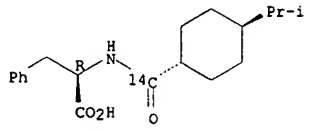
RN 475168-27-5 HCAPLUS
CN D-Phenylalanine, 4-chloro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



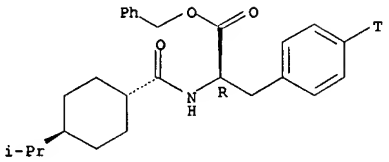
IT 475168-21-9P 475168-29-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(stereoselective preparation of [14C]- and [3H]DJN608 [Starlix])
RN 475168-21-9 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl-14C]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



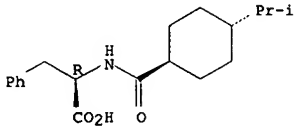
RN 475168-29-7 HCAPLUS
CN D-Phenylalanine-4-t, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 37 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 105816-04-4DP, Nateglinide, B crystal type
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and crystalline forms of)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

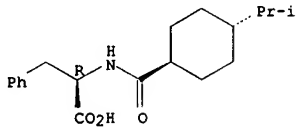
Absolute stereochemistry.



RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of Nateglinide

L4 ANSWER 38 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 105816-04-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and effect of cycloalkylcarboxamide derivs. as cysteine protease inhibitors)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

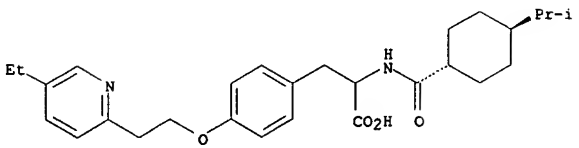
Absolute stereochemistry.



L4 ANSWER 39 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 321371-24-8P

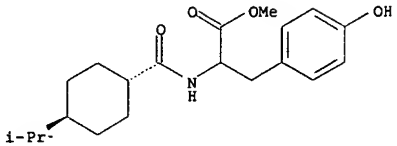
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of thiazolidinediones as insulinotropics and insulin sensitizers)
RN 321371-24-8 HCAPLUS
CN Tyrosine, O-[2-(5-ethyl-2-pyridinyl)ethyl]-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



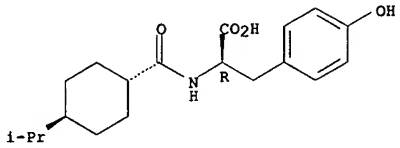
IT 321371-23-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of thiazolidinediones as insulinotropics and insulin sensitizers)
RN 321371-23-7 HCAPLUS
CN Tyrosine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



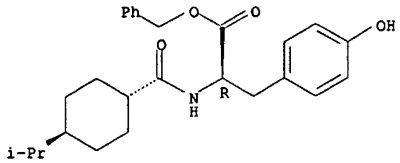
L4 ANSWER 40 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 183996-89-6P
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); SPN (Synthetic preparation); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation)
(structure of metabolites of AY4166 as hypoglycemic (Erratum))
RN 183996-89-6 HCAPLUS
CN D-Tyrosine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



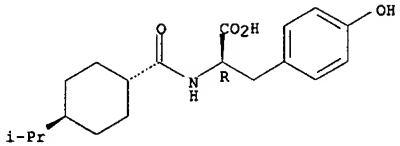
IT 183997-01-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(structure of metabolites of AY4166 as hypoglycemic (Erratum))
RN 183997-01-5 HCAPLUS
CN D-Tyrosine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 41 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 183996-89-6P
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); SPN (Synthetic preparation); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation)
(structure of metabolites of AY4166 as hypoglycemic)
RN 183996-89-6 HCAPLUS
CN D-Tyrosine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

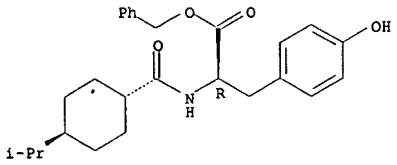
Absolute stereochemistry.



IT 183997-01-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(structure of metabolites of AY4166 as hypoglycemic)
RN 183997-01-5 HCAPLUS

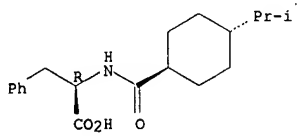
CN D-Tyrosine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



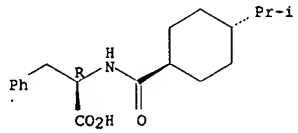
L4 ANSWER 42 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 105816-04-4P
RL: PNU (Preparation, unclassified); PREP (Preparation)
(preparation of trans-4-isopropylcyclohexanecarboxylic acid chloride as intermediate for antidiabetic agent by chlorination of the acid with P chloride)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



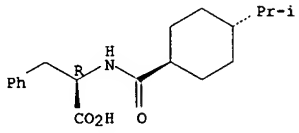
L4 ANSWER 43 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 105816-04-4P
RL: PREP (Preparation)
(crystals, stable, preparation of)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



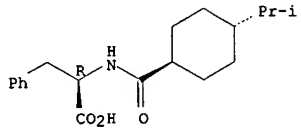
L4 ANSWER 44 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 105816-04-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and hypoglycemic activity of)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



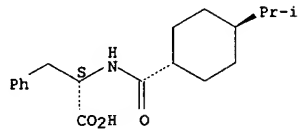
L4 ANSWER 45 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 105816-04-4P 105816-05-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as hypoglycemic)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



RN 105816-05-5 HCAPLUS
CN L-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

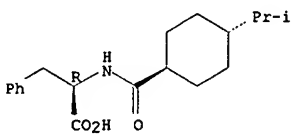
Absolute stereochemistry.



L4 ANSWER 46 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
IT 105816-04-4P 105816-05-5P

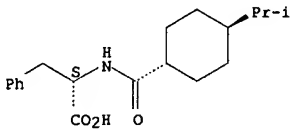
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as hypoglycemic)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



RN 105816-05-5 HCAPLUS
CN L-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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(FILE 'HOME' ENTERED AT 18:28:54 ON 02 MAY 2007)

FILE 'REGISTRY' ENTERED AT 18:29:05 ON 02 MAY 2007
L1 STRUCTURE UPLOADED
L2 5 S L1 SSS SAM
L3 101 S L1 SSS FULL

FILE 'HCAPLUS' ENTERED AT 18:29:57 ON 02 MAY 2007
L4 46 S L3/P

=> d l4 1-46 ibib abs

L4 ANSWER 1 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:14393 HCAPLUS
DOCUMENT NUMBER: 146:163387
TITLE: Preparation of H type nateglinide crystal
INVENTOR(S): Chen, Songnian; Feng, Qianjian; Yu, Yingmin
PATENT ASSIGNEE(S): Hangzhou Pollen Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 5pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1887858	A	20070103	CN 2006-10052617	20060721

PRIORITY APPLN. INFO.: CN 2006-10052617 20060721
OTHER SOURCE(S): CASREACT 146:163387
AB The title method comprises the steps of: (1) condensing trans-4-isopropylcyclohexanecarbonyl chloride with D-phenylalanine to obtain crude crystal of B type nateglinide, (2) dissolving the crude crystal in the solution of methanol, aminomethane and water (volume ratio of 60:20:20), heating to 40-60°C, adding 2% active carbon, decoloring for 7-15 min, filtrating, cooling to 10°C to precipitate, filtrating, washing with 40% ethanol till neutral, and drying to obtain H type nateglinide crystal, and (3) recrystg. the mother solution to obtain H type nateglinide crystal. The product of H type nateglinide crystal has good physiol. activity.

L4 ANSWER 2 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1339720 HCAPLUS
DOCUMENT NUMBER: 146:82189
TITLE: Preparation of L-threonine derivatives with high therapeutic index
INVENTOR(S): Chandran, V. Ravi
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 60pp., Cont.-in-part of U.S. Ser. No. 343,557.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006287244	A1	20061221	US 2006-442027	20060526
WO 2005046575	A2	20050526	WO 2004-US24901	20040729
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2006241017	A1	20061026	US 2006-343557	20060130

PRIORITY APPLN. INFO.: US 2003-491331P P 20030729
WO 2004-US24901 A2 20040729
US 2006-343557 A2 20060130
AB The invention is directed to novel therapeutic compds. comprised of an L-threonine bonded to a medicament or drug having a hydroxy, amino, carboxy or acylating function. These high-therapeutic index derivs. have the same utility as the drug from which they are made and they have enhanced pharmacol. and pharmaceutical properties, with the addnl. advantage of separating various enantiomeric and diastereomeric drugs into their individual isomers. The examples describe the synthesis and

activities of L-threonine derivs. of (±)- and (+)-(S)-ibuprofen, (±)- and (+)-(S)-ketoprofen, (-)-(S)-ketorolac, aspirin, and fenofibric acid. The synthesis and activity of several L-serine and L-hydroxyproline analogs were also described. Thus, the hydrochloride of (+)-(S)-ibuprofen ester of L-threonine was prepared, and its free base examined for analgesic, gastric mucosal irritation, toxicity, and pharmacokinetic properties.

L4 ANSWER 3 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:657506 HCAPLUS
DOCUMENT NUMBER: 145:103952
TITLE: Process for the preparation of nateglinide, preferably in B-form
INVENTOR(S): Vigano, Enrico; Pizzatti, Enrica; Lanfranconi, Simona; Molteni, Renato; Landonio, Ernesto
PATENT ASSIGNEE(S): Italy
SOURCE: U.S. Pat. Appl. Publ., 22 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006148902	A1	20060706	US 2005-28283	20050103
PRIORITY APPLN. INFO.:			US 2005-28283	20050103

OTHER SOURCE(S): CASREACT 145:103952
AB The invention relates to a process for the preparation of nateglinide, preferably in B-form, substantially free from the H-form, comprising three steps starting from (i) reaction in an organic solvent between D-phenylalanine Me ester or a salt and trans-4-isopropylcyclohexancarboxylic acid in the presence of an acyl chloride or carbonyldiimidazole, optionally isolating the nateglinide Me ester obtained and re-dissolving it in a second organic solvent, (ii) addition of water and alkali hydroxide to the reaction mixture and separation of the aqueous phase containing the alkali salt of nateglinide, and (iii) addition of hydrochloric acid to the aqueous phase from step (ii) to obtain nateglinide. In an example, the reaction was carried out in acetone in the presence of triethylamine and Et chloroformate and hydrolysis of nateglinide Me ester was carried out using toluene, tricaprylmethylammonium chloride, and aqueous potassium hydroxide to afford nateglinide in B-form (130.44°C).

L4 ANSWER 4 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:328161 HCAPLUS
DOCUMENT NUMBER: 145:173833
TITLE: Direct separation and enantioseparation of nateglinide stereoisomers by HPLC
AUTHOR(S): Yin, Yanjie; Zhang, Qiming; Li, Huiyi; Ning, Baoming; Liu, Wenying; Tian, Songjiu
CORPORATE SOURCE: China Pharmaceutical University, Nanjing, 210009, Peop. Rep. China
SOURCE: Yaowu Fenxi Zazhi (2005), 25(6), 657-659
CODEN: YFZADL; ISSN: 0254-1793
PUBLISHER: Yaowu Fenxi Zazhi Bianji Weiyuanhui
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB An HPLC method was developed to sep. the enantiomers of nateglinide as well as trans-nateglinide and cis-nateglinide. The nateglinide

enantiomers, trans-nateglinide and cis-nateglinide were directly separated on a HPLC chiral stationary phase consisting of the Kromasil TBB with hexane-2-propanol-acetic acid (95:5:0.2) as eluent and a flow rate of 0.6 mL·min-1 at 258 nm and 20°C. Three kinds of Nateglinide could be completely separated, and the resolns. were 2.38 and 1.85, resp. The method can be used for separating the nateglinide enantiomers, trans-nateglinide and cis-nateglinide and determining content of nateglinide.

L4 ANSWER 5 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1328488 HCAPLUS
DOCUMENT NUMBER: 144:51894
TITLE: One-pot process for the preparation of nateglinide
INVENTOR(S): Kankan, Rajendra Narayanrao; Rao, Dharmaraj Ramachandra; Singh, Manjinder; Birari, Dilip Ramdas
PATENT ASSIGNEE(S): Cipla Limited, India; Wain, Christopher Paul
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005121071	A1	20051222	WO 2005-GB2267	20050608
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005252002	A1	20051222	AU 2005-252002	20050608
CA 2570041	A1	20051222	CA 2005-2570041	20050608
EP 1765769	A1	20070328	EP 2005-750279	20050608
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
PRIORITY APPLN. INFO.:			GB 2004-13084	A 20040611
			WO 2005-GB2267	W 20050608

OTHER SOURCE(S): CASREACT 144:51894; MARPAT 144:51894
AB A one-pot process for the preparation of nateglinide is presented which comprises amidation of a C1-4 alkyl ester of D-phenylalanine, either as the free base or in salt form (typically the hydrochloride), with trans-4-isopropylcyclohexanecarboxylic acid or its acid halides to obtain a C1-4 alkyl ester of nateglinide, preferably the Me ester of nateglinide, followed by alkali (e.g., NaOH) saponification and acidification (e.g., HCl) to yield nateglinide (m.p. 128-131°).
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1261034 HCAPLUS
DOCUMENT NUMBER: 144:23128
TITLE: Stable nateglinide form b compositions via

crystallization
INVENTOR(S): Venkataraman, Sundaram; Narsapur, Sharat Pandurang; Kharkar, Manoj Ramesh; Bangarubabu, Rongali; Sandeep, Mohanty; Sayantani, Pyne; Raju, Kakarlapudi Ranga
PATENT ASSIGNEE(S): Dr. Reddy's Laboratories Ltd., India; Dr. Reddy's Laboratories, Inc.
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005113485	A2	20051201	WO 2005-US17664	20050520

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:
US 2004-572689P P 20040520
US 2004-586431P P 20040708
US 2005-644614P P 20050118

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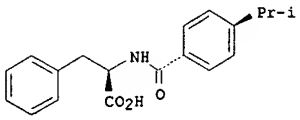

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AB A process for preparing nateglinide Form B comprises dissolving nateglinide (I) in a solvent and adding the solution, at temps. of 40-45°C, to a hydrocarbon liquid that is at temps. of 40-45°C. Then, water is added and the mixture is allowed to cool, producing crystals of nateglinide Form B.

L4 ANSWER 7 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1240947 HCAPLUS
DOCUMENT NUMBER: 144:11582
TITLE: Process for the preparation of polymorphic crystalline forms of nateglinide ammonium salt
INVENTOR(S): Wizel, Shlomit; Frenkel, Gustavo; Gome, Boaz
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals Usa, Inc.
SOURCE: PCT Int. Appl., 25 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005110972	A1	20051124	WO 2005-US16343	20050509

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2563793	A1	20051124	CA 2005-2563793	20050509
US 2006004102	A1	20060105	US 2005-126050	20050509
EP 1656339	A1	20060517	EP 2005-748381	20050509

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU

CN 1950331	A	20070418	CN 2005-80014509	20050509

PRIORITY APPLN. INFO.:
US 2004-569047P P 20040507
WO 2005-US16343 W 20050509

AB Anti-hyperglycemic polymorphic crystalline forms of nateglinide ammonium salt are prepared
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:841495 HCAPLUS
DOCUMENT NUMBER: 145:315230
TITLE: Synthesis of nateglinide analogs and their bioactivity determination
AUTHOR(S): Zhang, Jianxin; Dong, Junjun; Han, Han; Gong, Zehui; Huang, Shijie; Liu, Keliang
CORPORATE SOURCE: Institute of Pharmacology and Toxicology, Academy of Military Medical Sciences, Beijing, 100850, Peop. Rep. China
SOURCE: Zhongguo Yaowu Huaxue Zazhi (2004), 14(6), 335-339, 362
CODEN: ZYHZEF; ISSN: 1005-0108
PUBLISHER: Zhongguo Yaowu Huaxue Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
OTHER SOURCE(S): CASREACT 145:315230
AB Analogs of nateglinide [i.e., N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-D-phenylalanine] were synthesized, and their biol. activities were tested by glycemia levels in mice. The new compds. were synthesized using N-(isopropyl)piperazine, N-isopropyl-4-piperidinecarboxylic acid, trans-4-dimethylamino-1-cyclohexanecarboxylic acid and substituted phenylalanine as the starting materials. The biol. activities of the new compds. were tested by the glycemia levels in mice via drug administration

after forbiddance of food-intake and oral delivery of glucose. Forty-three new compds. were synthesized, and their structures were confirmed by elementary anal., IR, polarimetric anal., 1H-NMR and MS. One compound, 4-fluoro-N-[[4-(1-methylethyl)-1-piperazinyl]carbonyl]-L-phenylalanine monohydrochloride, showed significant hypoglycemic effect on glycemia of mice, and had an (S)-configuration at the chiral center, which was opposite to the control.

L4 ANSWER 9 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:476519 HCAPLUS
DOCUMENT NUMBER: 143:97635
TITLE: Improved process for the preparation of hypoglycemic agent nateglinide
INVENTOR(S): Zhong, Bohua; Wu, Bo; Yan, Yuan
PATENT ASSIGNEE(S): Toxic Drug Inst., Academy of Military Medical Science, PLA, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, No pp. given
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1517335	A	20040804	CN 2003-100559	20030117
PRIORITY APPLN. INFO.:			CN 2003-100559	20030117

OTHER SOURCE(S): CASREACT 143:97635
AB A scalable process for the preparation of nateglinide, a hypoglycemic agent, was reported. The key improvement is that the acylation of D-phenylalanine with 4-isopropylcyclohexanecarbonyl chloride was performed under a homogeneous condition using a mixture of dioxane or THF and H2O as solvent, largely increasing the yield. Other features include the use of cheap Pd/C instead of previously expensive PtO2 as hydrogenation catalyst in the reduction of 4-isopropylbenzoic acid into 4-isopropylcyclohexanecarboxylic acid. Purification of nateglinide by recrystn. in petroleum ether, hexane and cyclohexane or their mixts. is claimed.

L4 ANSWER 10 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:476518 HCAPLUS
DOCUMENT NUMBER: 143:26875
TITLE: Improved process for the preparation of hypoglycemic agent nateglinide
INVENTOR(S): Zhu, Qin; Pan, Junfang; Shi, Mingfeng
PATENT ASSIGNEE(S): Shanghai Huashuo Medicine Science & Technology Development Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, No pp. given
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1517334	A	20040804	CN 2003-114970	20030117
PRIORITY APPLN. INFO.:			CN 2003-114970	20030117

OTHER SOURCE(S): CASREACT 143:26875
AB A scalable process for the preparation of nateglinide, a hypoglycemic agent, was reported. The key improvement is that the acylation of D-phenylalanine with 4-isopropylcyclohexanecarbonyl chloride was performed under a homogeneous condition using a mixture of DMF and H2O as solvent, largely increasing the yield. Other features include the use of cheap Pd/C instead of previously expensive PtO2 as hydrogenation catalyst in the reduction of 4-isopropylbenzoic acid into 4-isopropylcyclohexanecarboxylic acid.

L4 ANSWER 11 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:467801 HCAPLUS
DOCUMENT NUMBER: 143:7982
TITLE: Process for the preparation of the crystalline B-form nateglinide from D-phenylalanine methyl ester and trans-4-isopropylcyclohexanecarboxylic acid
INVENTOR(S): Vigano', Enrico; Pizzati, Enrica; Lanfranconi, Simona; Molteni, Renato; Landonio, Ernesto
PATENT ASSIGNEE(S): A.M.S.A. Anonima Materie Sintetiche e Affini S.p.A., Italy
SOURCE: Eur. Pat. Appl., 32 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1535900	A1	20050601	EP 2003-27114	20031126
EP 1535900	B1	20061227		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 349418	T	20070115	AT 2003-27114	20031126
PRIORITY APPLN. INFO.:			EP 2003-27114 A	20031126

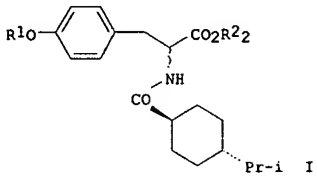
OTHER SOURCE(S): CASREACT 143:7982
AB A process for the preparation of nateglinide comprises: (I) the amidation reaction in a first organic solvent between D-phenylalanine Me ester, or a salt, and trans-4-isopropylcyclohexanecarboxylic acid and an acyl chloride, or carbonyldiimidazole, to obtain the nateglinide Me ester; (Ia) optionally isolating the nateglinide Me ester and redissolving it in a second organic solvent to give a solution; (II) addition of water and alkali hydroxide to the reaction mixture coming from step (I) without isolating the nateglinide Me ester, or, if applicable, to the solution of step (Ia), and separation of the aqueous phase containing the alkali salt of nateglinide; (III) addition of hydrochloric acid to the aqueous phase coming from step (II) to obtain nateglinide , wherein the organic solvent employed in step (II) is a water non-miscible solvent.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:414565 HCAPLUS
DOCUMENT NUMBER: 142:482315
TITLE: Preparation of alanine derivative as antidiabetics
INVENTOR(S): Yang, Yushe; Tang, Lei; Ji, Ruyun; Chen, Kaixian
PATENT ASSIGNEE(S): Shanghai Institute of Pharmacy, Chinese Academy of Sciences, Peop. Rep. China

SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 26 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1431197	A	20030723	CN 2003-115160	20030124
PRIORITY APPLN. INFO.:			CN 2003-115160	20030124

OTHER SOURCE(S): CASREACT 142:482315; MARPAT 142:482315
GI



I

AB Alanine derivs. I (R1 = 2-(1-indolyl)ethyl, 2-[N-(2-benzoxazolyl)-N-methyl]aminoethyl, 2-(N-methyl-N-(2-pyridinyl)]aminoethyl, 2-(4-methyl-2-phenyl-4-oxazolyl)ethyl, 4-trifluoromethylbenzyl, benzyl; R2 = H, alkyl) is prepared by condensation reaction of trans-4-isopropylcyclohexanecarboxylic acid N-succinimidyl ester with L- or D-tyrosine Me ester in inert solvent to obtain 3-(4-hydroxyphenyl)-2-(trans-isopropylcyclohexylcarboxamido)propanoic acid Me ester (II), Mitsunobu reaction with aromatic alc., and then hydrolysis with inorg. base solution The method may be prepared by (1) etherification of II with alkyl halide in alkaline medium; (2) hydrolysis of II; or (3) condensation reaction of II with amino-protected 2-methylaminoethanol, condensation reaction with 2-fluoropyridine, and hydrolysis with base. The alanine derivative and its salt may be used to prepare the medical prepns. for treating type II diabetes mellitus.

L4 ANSWER 13 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:283370 HCAPLUS
DOCUMENT NUMBER: 142:331961
TITLE: Mechanism-based targeted pancreatic beta cell imaging and therapy
INVENTOR(S): Yang, David J.; Oh, Chang-sok; Kohanim, Saady; Yu, Dong-Fang; Azhdarinia, Ali; Bryant, Jerry
PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005027981	A1	20050331	WO 2004-US30374	20040916
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004273911	A1	20050331	AU 2004-273911	20040916
CA 2539384	A1	20050331	CA 2004-2539384	20040916
US 2005100506	A1	20050512	US 2004-942615	20040916
EP 1675625	A1	20060705	EP 2004-788800	20040916
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
BR 2004014512	A	20061107	BR 2004-14512	20040916
CN 1867363	A	20061122	CN 2004-80030089	20040916
JP 2007505915	T	20070315	JP 2006-527025	20040916
NO 2006001645	A	20060411	NO 2006-1645	20060411
PRIORITY APPLN. INFO.:			US 2003-503683P P	20030917
			WO 2004-US30374 W	20040916

AB Compns. for imaging beta cells comprise chelator-antidiabetic agent conjugates and optionally chelated metals are described. Examples of agents are 99mTc-DTPA conjugated to nateglinide, glipizide, glyburide or glimepiride.
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

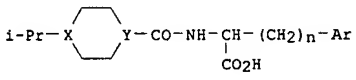
L4 ANSWER 14 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:249676 HCAPLUS
DOCUMENT NUMBER: 144:88520
TITLE: Syntheses and hypoglycemia activities of N-(trans-4-isopro-pylcyclohexylcarbonyl)-β-ring substituted phenylalanines
AUTHOR(S): Pan, Man-gen; Liang, Yuan-jun; Li, Bi-hai; Zhong, Bo-hua; Huang, Shi-jie; Gong, Ze-hui; Liu, Ke-liang
CORPORATE SOURCE: Institute of Pharmacology and Toxicology, Academy of Military Medical Sciences, Beijing, 100850, Peop. Rep. China
SOURCE: Zhongguo Yaowu Huaxue Zazhi (2003), 13(5), 249-253
CODEN: ZYHZEF; ISSN: 1005-0108
PUBLISHER: Zhongguo Yaowu Huaxue Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
OTHER SOURCE(S): CASREACT 144:88520
AB A series of title compds. were synthesized as nateglinide (N-(trans-4-isopropylcyclohexyl-1-carbonyl)-D-phenylalanine) analogs by condensation of substituted phenylalanine derivs. with trans-4-isopropylcyclohexanecarbonyl chloride. 3-Fluoro-N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-L-phenylalanine was prepared and showed hypoglycemic activity comparable to that of nateglinide.

L4 ANSWER 15 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:204069 HCAPLUS
DOCUMENT NUMBER: 142:482313
TITLE: Preparation of aromatic amino acid derivatives for treatment of blood sugar disorders
INVENTOR(S): Liu, Keliang; Pan, Mangen; Liang, Yuanjun; Zhong, Bohua; Li, Bihai; Huang, Shijie; Li, Xin; Dong, Huajin; Chi, Mugen
PATENT ASSIGNEE(S): Institute of Toxicant and Pharmaceuticals, Academy of Military Medical Science of PLA, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 41 pp. CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1453265	A	20031105	CN 2003-123272	20030425
PRIORITY APPLN. INFO.:			CN 2002-116715 A	20020426

OTHER SOURCE(S): CASREACT 142:482313; MARPAT 142:482313
GI



I

AB The aromatic amino acid derivs. I [n = 0, 1; X, Y = C, N; Ar = benzene ring substituted by one or more substituents (such as halo, NO2, OH, CO2H, CF3, trifluoromethoxy, methylenedioxy, methylenedithio, alkyl, alkenyl, cycloalkyl, cycloalkenyl, aryl, alkoxy, alkenoxy, phenoxy, benzyloxy, ester group, amino, amido), other aromatic ring, heterocyclic ring or its substituted derivative], useful for the treatment of blood sugar disorders, were prepared by acylation of 3-arylalanine HCl with 4-isopropylcyclohexylcarbonyl chloride or 1-isopropyl-4-piperidinylcarbonyl chloride. Thus, reaction of D-3-nitrophenylalanine hydrochloride with trans-4-isopropylcyclohexanecarbonyl chloride in THF in the presence of aqueous NaOH at room temperature for 5 h gave, after acidification with aqueous HCl, 71.1% N-(trans-4-isopropylcyclohexanecarbonyl)-D-3-nitrophenylalanine (II). II showed endothelin receptor antagonist activity at 10-9mol/L.

L4 ANSWER 16 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:59980 HCAPLUS
DOCUMENT NUMBER: 142:141289
TITLE: Crystalline form of nateglinide
INVENTOR(S): Frenkel, Gustavo; Gome, Boaz; Wizel, Shlomit
PATENT ASSIGNEE(S): Israel
SOURCE: U.S. Pat. Appl. Publ., 91 pp., Cont.-in-part of U.S. Ser. No. 622,905. CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005014836	A1	20050120	US 2003-746697	20031224
US 2004181089	A1	20040916	US 2003-622905	20030718
CA 2513753	A1	20040812	CA 2004-2513753	20040113
WO 2004067496	A1	20040812	WO 2004-US839	20040113
WO 2004067496	A9	20041209		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
EP 1511717	A1	20050309	EP 2004-701826	20040113
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1835912	A	20060920	CN 2004-80005672	20040113
US 2007004804	A1	20070104	US 2006-516363	20060905
PRIORITY APPLN. INFO.:			US 2003-442109P P	20030123
			US 2003-449791P P	20030224
			US 2003-479016P P	20030616
			US 2003-622905 A2	20030718
			US 2002-396904P P	20020718
			US 2002-413622P P	20020925
			US 2002-414199P P	20020926
			US 2002-423750P P	20021105
			US 2002-432093P P	20021210
			US 2002-432962P P	20021212
			US 2003-622999 A1	20030718
			WO 2003-US22375 A	20030718
			US 2003-693166 A	20031023
			US 2003-746697 A	20031224
			WO 2004-US839 W	20040113

AB Crystalline forms of nateglinide and processes for their preparation, as well as pharmaceutical formulations containing them and methods of administration are provided. A process for preparing crystalline form of nateglinide comprises the steps of(a) preparing a solution of nateglinide in Et acetate, (b) seeding the solution with nateglinide crystals, and (c) recovering the crystalline form as a precipitate The nateglinide obtained is more than about 99% pure. For example, nateglinide (5 g) was dissolved in acetonitrile, acetone, or Et acetate at about 55° in over about 15 min until a clear solution was obtained. The solvent was removed to dryness by evaporation at about 55°/20 to 30 mmHg to give dry nateglinide crystalline Form B. Also, nateglinide Form Z was prepared by treating 7.73 g of D-phenylalanine (PheOH) with 185 mL (3.5 equiv) of 3.5% NaOH at room temperature to afford a clear solution of the corresponding Na-salt. A solution of neat trans-4-isopropylcyclohexanecarboxyl chloride (IPCHAC, 9.02 g, 1.01 equiv) was added to the solution of Phe-OH obtained above, over 3 min, while stirring at room temperature The rest of the IPCHAC in the funnel was washed with toluene (1 mL) and added. The resulting mixture was stirred for 1 h, and was treated with 10% HCl (32 mL) to adjust the pH to 3, while stirring. The mixture was stirred for 1 h, and filtered. The solid was washed with water (200 mL) and sucked well to afford 33.3 g of the moist product, which lost weight after drying at 78°/2.2 mbar (Assay 98.4%, purity >99% , yield 86%).

L4 ANSWER 17 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:55192 HCAPLUS
DOCUMENT NUMBER: 142:156316
TITLE: A saponification and neutralization process for the preparation of chirally pure nateglinide from its lower alkyl esters and nateglinide polymorphic crystalline modifications
INVENTOR(S): Gazdag, Maria; Gizur, Tibor; Hegedus, Bela; Szemzo, Attila; Tarkanyi, Gabor; Toerley, Jozsef; Babjak, Monika
PATENT ASSIGNEE(S): Richter Gedeon Vegyeszeti Gyar Rt., Hung.
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005005373	A1	20050120	WO 2004-HU73	20040708
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
HU 200302174	A2	20050728	HU 2003-2174	20030710
EP 1651591	A1	20060503	EP 2004-743732	20040708
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR				
US 2007043117	A1	20070222	US 2006-564017	20060515
PRIORITY APPLN. INFO.:			HU 2003-2174 A	20030710
			WO 2004-HU73 W	20040708

OTHER SOURCE(S): CASREACT 142:156316
AB The preparation of chirally pure nateglinide by treating a nateglinide lower alkyl ester (e.g., Me ester) with an alkali base (e.g., sodium hydroxide) to yield an alkali salt and neutralizing liberating the salt by addition of an acid (e.g., aqueous HCl) is described as is the preparation of polymorphic crystalline modifications of nateglinide.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

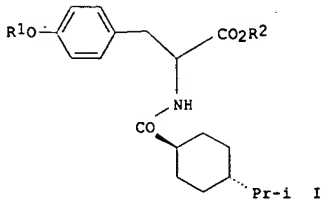
L4 ANSWER 18 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:937572 HCAPLUS
DOCUMENT NUMBER: 142:317044
TITLE: An efficient large scale synthesis of nateglinide
AUTHOR(S): Chandrasekhar, Batchu; Sawanth, Mangesh S.; Naik, Sameer J.; Gaikwad, Nandakumar B.; Kulkarni, Pramila V.; Bhirud, Shekar B.
CORPORATE SOURCE: Process Research and Development, Glenmark Research Centre, MIDC Mahape, Navi Mumbai, 400709, India
SOURCE: Organic Preparations and Procedures International (2004), 36(5), 459-467

CODEN: OPPIAK; ISSN: 0030-4948
PUBLISHER: Organic Preparations and Procedures, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:317044
AB Nateglinide was prepared as the desired H polymorph by reaction of trans-4-isopropylcyclohexanecarboxylic acid with ClCO2Et and treating the carbonate with D-phenylalanine.
REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 19 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:648495 HCAPLUS
DOCUMENT NUMBER: 141:157476
TITLE: Preparation of alanine compounds as antidiabetics
INVENTOR(S): Yang, Yushe; Tang, Lei; Ji, Ruyun; Chen, Kaixian
PATENT ASSIGNEE(S): Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Peop. Rep. China
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004067495	A1	20040812	WO 2003-CN96	20030128
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003303815	A1	20040823	AU 2003-303815	20030128
EP 1591440	A1	20051102	EP 2003-815509	20030128
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006513250	T	20060420	JP 2004-567216	20030128
US 2006154970	A1	20060713	US 2005-543091	20050722
PRIORITY APPLN. INFO.:			WO 2003-CN96 A	20030128

OTHER SOURCE(S): CASREACT 141:157476; MARPAT 141:157476
GI



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AB Alanine compds. I (R1 = H, alkyl, Ph, aryl, heteroaryl, etc.; R2 = H, alkyl), useful for treatment of type II diabetes, are prepared Thus, (2S)--2-[N-(trans-4-isopropylcyclohexylcarbonyl)amino]-3-[4-[2-(5-methyl-2-phenyl-4-oxazolyl)ethoxy]phenyl]propionic acid was prepared and showed insulin sensitizer activity.

L4 ANSWER 20 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:203799 HCAPLUS
DOCUMENT NUMBER: 140:241062
TITLE: Process for the formation of a crystalline polymorphic form of nateglinide
INVENTOR(S): Reguri, Buchi Reddy; Kadaboina, Rajasekhar; Polavarapu, Srinivas
PATENT ASSIGNEE(S): Reddy's Laboratories Limited, India; Reddy's Laboratories, Inc.
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004020396	A1	20040311	WO 2003-US26880	20030827
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IN 2002MA00631	A	20050304	IN 2002-MA631	20020828
AU 2003262928	A1	20040319	AU 2003-262928	20030827
US 2004077725	A1	20040422	US 2003-649380	20030827
PRIORITY APPLN. INFO.:			IN 2002-MA631 A	20020828
			WO 2003-US26880 W	20030827

AB A crystalline polymorphic form of nateglinide are described and its X-ray diffraction pattern presented.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 21 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:203709 HCAPLUS
DOCUMENT NUMBER: 140:259085
TITLE: Preparation of nateglinide inclusion complexes with cyclodextrins and their use in pharmaceutical compositions
INVENTOR(S): Niu, Zhanqi; Wang, Lifang; Chen, Yujie; Shen, Dongmin
PATENT ASSIGNEE(S): Zhongqi Pharmaceutical Technology (Shijiazhuang) Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004019989	A1	20040311	WO 2003-CN707	20030822
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 1478470	A	20040303	CN 2002-132321	20020827
AU 2003255130	A1	20040319	AU 2003-255130	20030822
PRIORITY APPLN. INFO.:			CN 2002-132321 A	20020827
			WO 2003-CN707 W	20030822

AB The invention relates to preparation of inclusion complexes of nateglinide, containing nateglinide and β-cyclodextrin and its derivates, particularly to nateglinide-β-cyclodextrin inclusion complexes. The preparing process comprises saturated solution method, ultrasonic method and grinding method. The inclusion complexes obtained have high stability and can be used in the manufacture of pharmaceutical formulations of nateglinide. For example, nateglinide-β-cyclodextrin (1:2) inclusion complex prepared by grinding the mixture of 10 mL nateglinide (0.0031 mol) ethanol solution and 7g β-cyclodextrin (0.0062 mol), was incorporated into tablets together with starch, crosslinked CMC and magnesium stearate.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 22 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:182826 HCAPLUS
DOCUMENT NUMBER: 140:199745
TITLE: Synthesis and purification of nateglinide
INVENTOR(S): Naik, Samir Jaivant; Kulkarni, Pramila Vijay; Gaikwad, Nandkumar Baburao; Sawant, Mangesh Shivram; Bhirud, Shekhar; Batchu, Chandrasekhar
PATENT ASSIGNEE(S): Glenmark Pharmaceuticals Limited, India
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004018408	A1	20040304	WO 2003-IB3270	20030812
WO 2004018408	A8	20050310		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IN 2002MU00773	A	20040605	IN 2002-MU773	20020826
AU 2003263386	A1	20040311	AU 2003-263386	20030812
PRIORITY APPLN. INFO.:			IN 2002-MU773 A	20020826
			WO 2003-IB3270 W	20030812

OTHER SOURCE(S): CASREACT 140:199745; MARPAT 140:199745

AB N-[(trans-4-isopropylcyclohexyl)carbonyl]-D-phenylalanine (nateglinide) was prepared by reaction of trans-4-isopropylcyclohexylcarboxylic acid with an alkyl chloroformate in a ketonic solvent in the presence of a base at -20 to 30°C and reaction of the mixed anhydride product with an aqueous alkali salt solution of D-phenylalanine. An example shows the synthesis of nateglinide by using triethylamine and Et chloroformate in acetone (97% pure following HPLC).

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 23 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:80637 HCAPLUS
DOCUMENT NUMBER: 140:151932
TITLE: Preparation of polymorphic forms of nateglinide
INVENTOR(S): Yahalomi, Ronit; Shapior, Evgeny; Dolitzky, Ben-zion; Gozlan, Yigael; Gome, Boaz
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceutical Usa, Inc.
SOURCE: PCT Int. Appl., 130 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004009532	A1	20040129	WO 2003-US22375	20030718
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

US 2004152782	A1	20040805	US 2003-614266	20030703
US 6861553	B2	20050301		
CA 2492644	A1	20040129	CA 2003-2492644	20030718
AU 2003253971	A1	20040209	AU 2003-253971	20030718
US 2004116526	A1	20040617	US 2003-623237	20030718
US 7148376	B2	20061212		
EP 1467964	A1	20041020	EP 2003-765665	20030718
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005014949	A1	20050120	US 2003-623290	20030718
US 2005075400	A1	20050407	US 2003-622999	20030718
CN 1723190	A	20060118	CN 2003-821921	20030718
JP 2006511614	T	20060406	JP 2005-505521	20030718
CA 2513753	A1	20040812	CA 2004-2513753	20040113
WO 2004067496	A1	20040812	WO 2004-US839	20040113
WO 2004067496	A9	20041209		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
EP 1511717	A1	20050309	EP 2004-701826	20040113
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1835912	A	20060920	CN 2004-80005672	20040113
US 2007004804	A1	20070104	US 2006-516363	20060905
PRIORITY APPLN. INFO.:			US 2002-396904P P	20020718
			US 2002-413622P P	20020925
			US 2002-414199P P	20020926
			US 2002-423750P P	20021105
			US 2002-432093P P	20021210
			US 2002-432962P P	20021212
			US 2003-442109P P	20030123
			US 2003-449791P P	20030224
			US 2003-479016P P	20030616
			US 2003-614266 A	20030703
			US 2002-393495P P	20020703
			US 2003-622905 A	20030718
			US 2003-622999 A1	20030718
			WO 2003-US22375 W	20030718
			US 2003-693166 A	20031023
			US 2003-746697 A	20031224
			WO 2004-US839 W	20040113

AB The invention discloses the preparation of 26 characterized forms of nateglinide (forms A, C, D, F, G, I, J, K, L, M, N, O, P, Q, T, U, V, Y, α, β, γ, δ, ε, σ, Θ and Ω). Most of the forms are solvates (with the exception of forms L, P, U, α, δ and σ). Polymorphic forms are characterized by their mp, DSC, XRPD, FTIR; form interconversion is also discussed. For example, D-phenylalanine is reacted with trans-[[4-(isopropyl)cyclohexanee]carbonyl]chloride (i. NaOHaq; ii. H2SO4). The wet cake of nateglinide is dissolved in EtOAc, the aqueous phase is removed and the resulting solution heated to 50° under reduced pressure and added to hot heptane. The resulting solution is cooled and seeded with the B-form to afford the δ-form (33% yield).

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 24 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:41431 HCAPLUS

DOCUMENT NUMBER: 140:94292
TITLE: Process for preparing nateglinide and its intermediates
INVENTOR(S): Yahalomi, Ronit; Shapiro, Evgeny; Dolitzky, Ben-zion; Gozlan, Yigael
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals Usa, Inc.
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004005240	A1	20040115	WO 2003-US21238	20030703
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003256454	A1	20040123	AU 2003-256454	20030703
EP 1487782	A1	20041222	EP 2003-763310	20030703
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1671649	A	20050921	CN 2003-817439	20030703
US 2004116526	A1	20040617	US 2003-623237	20030718
US 7148376	B2	20061212		
US 2005014949	A1	20050120	US 2003-623290	20030718
US 2005075400	A1	20050407	US 2003-622999	20030718
CN 1723190	A	20060118	CN 2003-821921	20030718
US 2007004804	A1	20070104	US 2006-516363	20060905

PRIORITY APPLN. INFO.:

US 2002-393495P	P	20020703
US 2002-396904P	P	20020718
US 2002-413622P	P	20020925
US 2002-414199P	P	20020926
US 2002-423750P	P	20021105
US 2002-432093P	P	20021210
US 2002-432962P	P	20021212
US 2003-442109P	P	20030123
US 2003-449791P	P	20030224
US 2003-479016P	P	20030616
WO 2003-US21238	W	20030703
US 2003-622999	A1	20030718

OTHER SOURCE(S): CASREACT 140:94292
AB A process for the preparation of nateglinide involves converting trans-4-isopropylcyclohexanecarboxylic acid into the acid chloride by reaction with thionyl chloride in the presence of an organic amide and acylation of a suitable salt of D-phenylalanine with the acid chloride in a single or two phase system or in water free of a co-solvent.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 25 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:892741 HCAPLUS
DOCUMENT NUMBER: 139:369757
TITLE: Process for the preparation of a crystal polymorphic form of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (nateglinide)
INVENTOR(S): Rajamahendra, Shanmughasamy; Aswathanarayanappa, Chandrashekar; Puthiaparampil, Tom Thomas; Sridharan, Madhavan; Ganesh, Sambasivam
PATENT ASSIGNEE(S): Biocon India Limited, India
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003093222	A1	20031113	WO 2002-IN114	20020429
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2481322	A1	20031113	CA 2002-2481322	20020429
AU 2002304281	A1	20031117	AU 2002-304281	20020429
EP 1499586	A1	20050126	EP 2002-733208	20020429
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
HU 200500259	A2	20050628	HU 2005-259	20020429
US 2005165108	A1	20050728	US 2003-508364	20020429
JP 2005523933	T	20050811	JP 2004-501362	20020429

PRIORITY APPLN. INFO.:

WO 2002-IN114	W	20020429

AB Novel polymorph Form C of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (I; i.e., nateglinide) is produced having a different IR spectrum and X-ray diffraction patterns (presented) from previously known forms of I.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 26 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:837030 HCAPLUS
DOCUMENT NUMBER: 139:341723
TITLE: Novel nateglinide crystals
INVENTOR(S): Koguchi, Yoshihito; Nakao, Tomoko; Sumikawa, Michito
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003087039	A1	20031023	WO 2003-JP4686	20030414
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003236243	A1	20031027	AU 2003-236243	20030414
EP 1496048	A1	20050112	EP 2003-746474	20030414
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005101672	A1	20050512	US 2004-965171	20041015
PRIORITY APPLN. INFO.:			JP 2002-111963 A	20020415
			WO 2003-JP4686 W	20030414

AB A type crystal (powder X-ray diffraction main peaks: 4.4°, 5.2°, 15.7°, 18.5° (2 theta)), M type crystal (powder X-ray diffraction main peaks: 6.0°, 14.2°, 15.2°, 18.8° (2 theta)), and P type crystal (powder X-ray diffraction main peaks: 4.8°, 5.3°, 14.3°, 15.2° (2 theta)) of nateglinide, which are all novel crystals, can be prepared by a method comprising dissolving nateglinide in a solvent exhibiting high solubility for nateglinide and then adding a solvent exhibiting poor solubility for nateglinide or dissolving nateglinide in a mixed solvent comprising a solvent exhibiting high solubility for nateglinide and a solvent exhibiting poor solubility for nateglinide and then cooling the resulting nateglinide solution to precipitate crystals, subjecting the product to filtration, and then drying at a specific temperature Nateglinide is a known antidiabetic.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 27 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:737716 HCAPLUS
DOCUMENT NUMBER: 139:230996
TITLE: Preparation and properties of nateglinide salts
INVENTOR(S): Sutton, Paul Allen; Vivilecchia, Richard Victor; Parker, David John; De La Cruz, Marilyn
PATENT ASSIGNEE(S): Novartis Ag, Switz.; Novartis Pharma Gmbh
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003076393	A1	20030918	WO 2003-EP2447	20030310
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW				

RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
CA 2478599	A1	20030918	CA 2003-2478599	20030310
AU 2003214112	A1	20030922	AU 2003-214112	20030310
EP 1483232	A1	20041208	EP 2003-709769	20030310
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003008316	A	20041228	BR 2003-8316	20030310
JP 2005519949	T	20050707	JP 2003-574615	20030310
CN 1642904	A	20050720	CN 2003-805803	20030310
US 2005234129	A1	20051020	US 2004-507255	20040928
PRIORITY APPLN. INFO.:			US 2002-363178P P	20020311
			WO 2003-EP2447 W	20030310

AB The invention relates to salts of nateglinide having specified properties (m.ps., solubilities, X-ray diffraction patterns) for use in pharmaceutical compns. for preventing or treating diabetes, cardiovascular diseases, etc. Nateglinide Na, K, Ca, Mg, N-methyl-D-glucamine, TRIS, lysine, and ammonium salts were prepared and their properties tabulated.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 28 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:76738 HCAPLUS
DOCUMENT NUMBER: 138:137033
TITLE: Oxidative process and catalysts for the manufacture of para-substituted benzoic acids from their corresponding aldehydes
INVENTOR(S): Girgis, Michael John; Shekhar, Ratna
PATENT ASSIGNEE(S): Novartis AG, Switz.
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003008367	A2	20030130	WO 2002-US22631	20020716
WO 2003008367	A3	20030410		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003023115	A1	20030130	US 2002-196600	20020715
US 6740776	B2	20040525		
AU 2002313681	A1	20030303	AU 2002-313681	20020716
PRIORITY APPLN. INFO.:			US 2001-305648P P	20010716
			WO 2002-US22631 W	20020716

OTHER SOURCE(S): CASREACT 138:137033; MARPAT 138:137033

AB A low-temperature process for preparing aromatic acids 4-(R1R2CH)C6H4CO2H [R1, R2 = H,

C1-8 (un)branched alkyl, cycloalkyl; e.g., 4-isopropylbenzoic acid] comprises oxidizing the corresponding aromatic aldehyde 4-(R1R2CH)C6H4CHO (e.g., 4-isopropylbenzaldehyde) with a gas having an oxygen content of 1-100% at 20° to <100° in the presence of a supported Group VIII metal catalyst (e.g., Pt/C), and using a solvent having a flash point >95°C and/or a m.p. <55°, provided that the flash point of the solvent is greater than the reaction temperature

L4 ANSWER 29 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:62632 HCAPLUS
DOCUMENT NUMBER: 138:73015
TITLE: Synthesis process for trans-4-isopropylcyclohexanecarboxylic acid
INVENTOR(S): Gu, Lianquan; An, Linkun; Ma, Lin; Guo, Xindong; Huang, Zhishu
PATENT ASSIGNEE(S): Zhongshan Univ., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 6 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1319583	A	20011031	CN 2001-107459	20010116
PRIORITY APPLN. INFO.:			CN 2001-107459	20010116

OTHER SOURCE(S): CASREACT 138:73015
AB The process comprises hydrogenating cumic acid in acetic acid in the presence of PtO2, recovering solvent, treating with 10-35% inorg. base (such as Ba(OH)2, Mg(OH)2, KOH, or NaOH) solution at 50-150° for 10-20 h, neutralizing with HCl to pH 2, crystallizing, filtering, and recrystg. in methanol.

L4 ANSWER 30 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:30017 HCAPLUS
DOCUMENT NUMBER: 139:210299
TITLE: Study on separation of cis-isomer of nateglinide by high-pressure liquid chromatographic method
AUTHOR(S): Yan, Xiaoyan; Hu, Xin; Cao, Guoying; He, Xiaorong; Yin, Qi
CORPORATE SOURCE: Beijing Hospital, Ministry of Public Health, Beijing, 100730, Peop. Rep. China
SOURCE: Zhongguo Yaoxue Zazhi (Beijing, China) (2002), 37(6), 444-446
CODEN: ZYZAEU; ISSN: 1001-2494
PUBLISHER: Zhongguo Yaoxue Zazhishe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB A high-pressure liquid chromatog. method for the separation of cis-isomer of nateglinide was established on Phenomenex Luna C18 column (5 μm, 4.6 mm x 250 mm) with UV detection at 214 nm and room temperature The mobile phase was consisted of (A) acetonitrile and (B) 0.03 mol L-1 phosphate buffer (pH 2.5, 65:35, volume/volume). The resolution factors were at least 1.5. The limits of detection and quantitation limit was 0.06 and 0.18 μg mL-1, resp. The method is useful in separation and determination of the cis-isomer from nateglinide.

L4 ANSWER 31 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:609152 HCAPLUS
DOCUMENT NUMBER: 138:254901
TITLE: a new synthesis method of nateglinide as antidiabetic drug
AUTHOR(S): Wang, Dun; Liang, Yiheng; Gong, Ping; Zhao, Yanfang
CORPORATE SOURCE: School of Pharmaceutical Engineering, Shenyang Pharmaceutical University, Shenyang, 110016, Peop. Rep. China
SOURCE: Zhongguo Yaowu Huaxue Zazhi (2002), 12(2), 94-96
CODEN: ZYHZEF; ISSN: 1005-0108
PUBLISHER: Zhongguo Yaowu Huaxue Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
OTHER SOURCE(S): CASREACT 138:254901
AB A new antidiabetic drug-nateglinide was synthesized from isopropylbenzene by Friedel-Crafts reaction, chloroform reaction, catalytic hydrogenation to obtain trans-4-isopropylhexanecarboxylic acid, acylation of D-phenylalanine Et ester, hydrolysis to obtain nateglinide B-type crystal, and crystal-conversion. The total yield was 9.8%.

L4 ANSWER 32 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:332157 HCAPLUS
DOCUMENT NUMBER: 136:340998
TITLE: Process for producing B-form nateglinide crystals
INVENTOR(S): Sumikawa, Michito; Maruo, Makoto; Miyazaki, Kazuo; Nishina, Shigehiro; Matsuzawa, Yukiko
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: PCT Int. Appl., 9 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002034713	A1	20020502	WO 2001-JP9293	20011023
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 200196001	A	20020506	AU 2001-96001	20011023
CA 2426745	A1	20030423	CA 2001-2426745	20011023
EP 1334964	A1	20030813	EP 2001-976819	20011023
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001014846	A	20040225	BR 2001-14846	20011023
RU 2275354	C2	20060427	RU 2003-111948	20011023
US 2003229249	A1	20031211	US 2003-421888	20030424
IN 2003CN00609	A	20050415	IN 2003-CN609	20030424
PRIORITY APPLN. INFO.:			JP 2000-324375 A	20001024
			WO 2001-JP9293 W	20011023

AB A process for producing B-form nateglinide crystals containing substantially no H-form crystals comprises the steps of drying wet crystals of a nateglinide solvate at a low temperature until the solvent disappears and then causing them to undergo a crystal transition. Nateglinide is a known antidiabetic. By this process, B-form nateglinide crystals can be produced on an industrial scale.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 33 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:314896 HCAPLUS
DOCUMENT NUMBER: 136:325825
TITLE: Process for producing nateglinide crystals
INVENTOR(S): Takahashi, Daisuke; Nishi, Seiichi; Takahashi, Satoji
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002032854	A1	20020425	WO 2001-JP9069	20011016
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 200194265	A	20020429	AU 2001-94265	20011016
CA 2425538	A1	20030410	CA 2001-2425538	20011016
EP 1334963	A1	20030813	EP 2001-974875	20011016
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001014729	A	20031014	BR 2001-14729	20011016
RU 2273629	C2	20060410	RU 2003-111021	20011016
CN 1769263	A	20060510	CN 2005-10118852	20011016
TW 251588	B	20060321	TW 2001-90125697	20011017
IN 2003CN00537	A	20050415	IN 2003-CN537	20030411
US 2004030182	A1	20040212	US 2003-418105	20030418
US 7208622	B2	20070424		

PRIORITY APPLN. INFO.:
JP 2000-317604 A 20001018
CN 2001-820658 A3 20011016
WO 2001-JP9069 W 20011016

OTHER SOURCE(S): CASREACT 136:325825
AB A process for producing nateglinide crystals comprises reacting trans-4-isopropylcyclohexylcarbonyl chloride with D-phenylalanine in a mixed solvent consisting of a ketone solvent and water in the presence of an alkali to obtain a reaction mixture containing nateglinide, adding an acid to the reaction mixture to make it acidic, and regulating (a) the temperature to 58° to 72° and (b) and the ketone solvent concentration to > 8 weight% and < 22 weight%, to conduct crystallization Nateglinide is a known antidiabetic.

The process is an industrially advantageous method for crystallizing nateglinide.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 34 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:314895 HCAPLUS
DOCUMENT NUMBER: 136:340997
TITLE: Process for preparation of acylphenylalanines
INVENTOR(S): Sumikawa, Michito; Ohgane, Takao
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002032853	A1	20020425	WO 2001-JP9068	20011016
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 200194264	A	20020429	AU 2001-94264	20011016
CA 2425533	A1	20030410	CA 2001-2425533	20011016
EP 1334962	A1	20030813	EP 2001-974874	20011016
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001014728	A	20031014	BR 2001-14728	20011016
RU 2287520	C2	20061120	RU 2003-111012	20011016
TW 575541	B	20040211	TW 2001-90125695	20011017
IN 2003CN00536	A	20050415	IN 2003-CN536	20030411
US 2004024219	A1	20040205	US 2003-418102	20030418
US 7030268	B2	20060418		
US 2006155143	A1	20060713	US 2005-319177	20051228

PRIORITY APPLN. INFO.:
JP 2000-317603 A 20001018
WO 2001-JP9068 W 20011016
US 2003-418102 A1 20030418

OTHER SOURCE(S): CASREACT 136:340997
AB This document discloses a process for preparing easily and simply high-purity acylphenylalanines extremely useful as raw materials of drugs or the like, characterized by reacting an acid chloride with phenylalanine in a mixed solvent consisting of an organic solvent and water under conditions made alkaline with potassium hydroxide.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

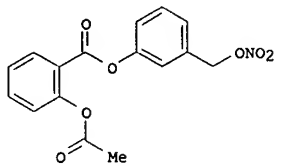
L4 ANSWER 35 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:293592 HCAPLUS
DOCUMENT NUMBER: 136:325420
TITLE: Drugs for diabetes, especially type 2, comprising an

antiinflammatory or analgesic drug, selected bivalent linkers, and a nitrate ester
INVENTOR(S): Del Soldato, Piero
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002030867	A2	20020418	WO 2001-EP11665	20011009
WO 2002030867	A3	20020725		
W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IT 2000MI2201	A1	20020412	IT 2000-MI2201	20001012
IT 1319201	B1	20030926		
CA 2425655	A1	20020418	CA 2001-2425655	20011009
AU 200214006	A	20020422	AU 2002-14006	20011009
EP 1324974	A2	20030709	EP 2001-982414	20011009
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004511456	T	20040415	JP 2002-534256	20011009
US 2004023890	A1	20040205	US 2003-398511	20030411

PRIORITY APPLN. INFO.: IT 2000-MI2201 A 20001012
WO 2001-EP11665 W 20011009

OTHER SOURCE(S): MARPAT 136:325420
GI



II

AB Useful for the treatment of diabetes, particularly type 2, are compds. or salts thereof, having the following general formula A-(B)n-(C)m-NO2 [I; wherein A = radical of a drug having an antiinflammatory or analgesic activity; B = bivalent linking group wherein the precursor must meet certain tests described in the application; C = another defined bivalent linking group; n and m = 0 or 1, provided that (n + m) = 1 or 2]. I can be used in conjunction with other antidiabetic drugs, particularly insulin. I increase the direct antidiabetic effect of insulin, and reduce complications of diabetes, particularly vascular diseases, retinopathies, neuropathies, etc.. The values of n and m, i.e., the presence or absence

of bivalent linkers B and C, alone or in combination, are based on performance of the precursors of the linkers in certain tests (no data). These tests are designated as follows: (test 4A): inhibition by > 15% of hemolysis of rat erythrocytes induced by cumene hydroperoxide; (test 5): inhibition of radical production by ≥ 50% in the oxidative degradation of desoxyribose in aqueous Fe2+(NH4)2(SO4)2/thiobarbituric acid solution; and (test 4): inhibition by ≥ 50% of DPPH-induced radical production in MeOH solution For instance, acetylsalicylic acid chloride was esterified with 3-(hydroxymethyl)phenol (80%), followed by nitation of the resultant Ph ester with HNO3/H2SO4 (82%), to give invention compound II, which is thus the 3-(nitrooxymethyl)phenyl ester of aspirin. When tested on isolated aorta from insulin-resistant rats, compound II at a concentration of 10-4 M gave 70% vasorelaxation, relative to non-insulin-resistant controls. This effect was unchanged by the presence or absence of the irreversible NO synthetase inhibitor LNNA. In contrast, both Na nitroprussiate and the indomethacin analog of II, known NO donors, were inactive, and the antidiabetic drug metformin was inactivated by LNNA.

L4 ANSWER 36 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:174779 HCAPLUS
DOCUMENT NUMBER: 137:370326
TITLE: Synthesis of [14C]- and [3H]DJN608 [STARLIX]
AUTHOR(S): Ray, T.; Ciszewska, G.; Wu, A.; Jones, L.
CORPORATE SOURCE: DMPK-Isotope Section, Novartis Pharmaceuticals, E. Hanover, NJ, USA
SOURCE: Synthesis and Applications of Isotopically Labelled Compounds, Proceedings of the International Symposium, 7th, Dresden, Germany, June 18-22, 2000 (2001), Meeting Date 2000, 228-231. Editor(s): Pleiss, Ulrich; Voges, Rolf. John Wiley & Sons Ltd.: Chichester, UK.
CODEN: 69CIJC; ISBN: 0-471-49501-8
DOCUMENT TYPE: Conference
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:370326
AB A novel oral medication for treating type 2 diabetes is trans-N-[[4-(1-methylethyl)cyclohexyl]-carbonyl]-D-phenylalanine, DJN608 [Starlix]. The key step in the synthesis of [14C]DJN608 was the catalytic reduction of [carboxy-14C]cumic acid in the presence of PtO2 at 55 psi of hydrogen in acetic acid to give cis/trans-4-isopropylcyclohexane-[14C]carboxylic acid in 3:1 ratio. Alternatively methods for preparing this mixture of cis- and trans- acids (3:1) are presented. Tritiated DJN608 was prepared by reduction of the corresponding chloro derivative with tritium gas in the presence of 10% palladium on carbon.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

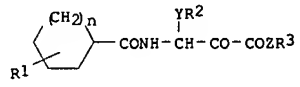
L4 ANSWER 37 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:130037 HCAPLUS
DOCUMENT NUMBER: 137:325603
TITLE: Synthesis of Nateglinide
AUTHOR(S): Zhu, Xue-yan; Peng, Ka; Wang, Xiao-qin; Yang, Li-ping
CORPORATE SOURCE: Dep. Chem., East China Normal Univ., Shanghai, 200062, Peop. Rep. China
SOURCE: Hecheng Huaxue (2001), 9(6), 537-540
CODEN: HEHUE2; ISSN: 1005-1511

PUBLISHER: Hecheng Huaxue Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
OTHER SOURCE(S): CASREACT 137:325603
AB Title compound, a new antidiabetes medicine, was synthesized from iso-propylbenzene in seven steps, giving the product with overall yield 22%.

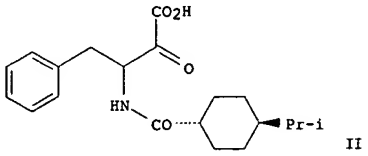
L4 ANSWER 38 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:38482 HCAPLUS
DOCUMENT NUMBER: 134:100592
TITLE: Preparation and effect of cycloalkylcarboxamide derivatives as cysteine protease inhibitors
INVENTOR(S): Sato, Masaaki; Mukoyama, Harunobu; Kobayashi, Junichi; Tsuyuki, Shogo; Tokutake, Katsunori; Akabane, Satoshi
PATENT ASSIGNEE(S): Kissei Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 27 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001011037	A	20010116	JP 1999-188275	19990701
PRIORITY APPLN. INFO.:			JP 1999-188275	19990701
OTHER SOURCE(S):	MARPAT 134:100592			

GI



I

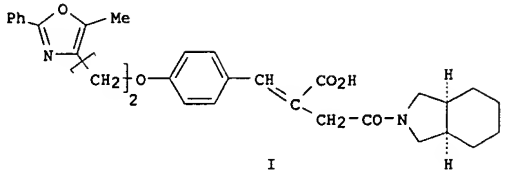


II

AB Title compds. [I; R1 = alkyl; Y = alkylene; R2 = OH, aryl, aryl alkoxy; R3 = H, alkyl, aryl, pyridyl, arylalkyl, pyridylalkyl; Z = O, NH; n = integer 1-3] and stereoisomers are prepared and possesses the cysteine protease

inhibitory effect. Title compds. are useful in prevention of arthritis, Alzheimer's disease, rheumatism and osteoporosis. Thus, the title compound II was prepared and tested.

L4 ANSWER 39 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:840649 HCAPLUS
DOCUMENT NUMBER: 134:110109
TITLE: Hybridization of non-sulfonylurea insulin secretagogue and thiazolidinedione-derived insulin sensitizer
AUTHOR(S): Kitajima, Hiroshi; Nakamura, Mitsuharu; Tamakawa, Hiroki; Goto, Nobuharu
CORPORATE SOURCE: Department of Discovery Research, Welfide Corporation, Hirakata, 573-1153, Japan
SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(21), 2453-2456
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Hybrid compds. of non-sulfonylurea insulinotropic agents and thiazolidinedione-derived insulin-sensitizing agents were designed and synthesized. The benzylidenesuccinic acid derivative I was equal both to nateglinide in potency of insulin-releasing activity and to pioglitazone in insulin-sensitizing activity.
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 40 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:228845 HCAPLUS
DOCUMENT NUMBER: 126:220267
TITLE: Structure determination of metabolites isolated form urine and bile after administration of AY4166, a novel D-phenylalanine-derivative hypoglycemic agent. [Erratum to document cited in CA126:325]
AUTHOR(S): Takesada, Hiroko; Matsuda, Keizo; Ohtake, Ryoko; Mihara, Ryuichi; Ono, Ichiro; Tanaka, Kenzo; Naito, Masaki; Yatagai, Masanobu; Suzuki, Ei-Ichiro
CORPORATE SOURCE: Central Research Laboratories, Ajinomoto Co., Inc., Kawasaki, 210, Japan
SOURCE: Bioorganic & Medicinal Chemistry (1997), 5(3), 637
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal

LANGUAGE: English
AB On page 1771 (column 2, line 26) and 1772 (column 1, line 2), the functional group of M2 in Figure 1, which was converted from one of two methyl groups of AY4166, should read hydroxylmethyl instead of methoxyl. On page 1776, column 2, in the parentheses of the fourth line from last, 60 mg/kg should read 60 mg/man.

L4 ANSWER 41 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:702133 HCAPLUS
DOCUMENT NUMBER: 126:325
TITLE: Structure determination of metabolites isolated from urine and bile after administration of AY4166, a novel D-phenylalanine-derivative hypoglycemic agent
AUTHOR(S): Takesada, Hiroko; Matsuda, Keizo; Ohtake, Ryoko; Mihara, Ryuichi; Ono, Ichiro; Tanaka, Kenzo; Naito, Masaki; Yatagai, Masanobu; Suzuki, Ei-ichiro
CORPORATE SOURCE: Central Research Laboratories, Ajinomoto Co., Inc., Kawasaki, 210, Japan
SOURCE: Bioorganic & Medicinal Chemistry (1996), 4(10), 1771-1781
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Mol. structures of 10 metabolites, which were isolated from urine (M1-M8) or bile (M9 and M10) after administration of AY4166 (N-(trans-4-isopropylcyclohexanecarbonyl)-D-phenylalanine), with hypoglycemic activity, were elucidated by mass spectrometry and NMR. Four of these (M1, M2, M3 and M8) were hydroxyl derivs. of AY4166, 2 (M9 and M10) were carboxylate derivs. via oxidation of M2 and M3, 3 (M4, M5 and M6) were glucuronic acid conjugates and the other (M7) was a dehydro derivative The structures for M1, M2, M3, M7, M8, M9 and M10 were confirmed by the coincidence of the retention time of HPLC, MS and 1H-NMR spectra between the isolated metabolites and authentic synthesized substances. For 3 glucuronic acid conjugates, M4, M5 and M6, structural confirmation was performed by a selective enzymic digestion with β-glucuronidase. M1 and M2/3 were about 5-6 and 3-fold less potent than AY4166, resp., and M7 was almost as potent as AY4166.

L4 ANSWER 42 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:468819 HCAPLUS
DOCUMENT NUMBER: 123:55430
TITLE: Preparation of trans-4-isopropylcyclohexanecarboxylic acid chloride
INVENTOR(S): Matsuzawa, Toshihiro; Irie, Yasuo
PATENT ASSIGNEE(S): Ajinomoto KK, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 3 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 07017899	A	19950120	JP 1993-163426	19930701
PRIORITY APPLN. INFO.:			JP 1993-163426	19930701

OTHER SOURCE(S): CASREACT 123:55430
AB The title compound (I), useful as an intermediate for antidiabetic

N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine, is prepared by treatment of trans-4-isopropylcyclohexanecarboxylic acid (II) with P chloride. II was treated with PCl5 in 1,2-dichloroethane at 40° for 3 h to give 94% I and 0% the cis-isomer, whereas cis-isomer was detected, when SOCl2 was used instead of PCl5.

L4 ANSWER 43 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:261002 HCAPLUS
DOCUMENT NUMBER: 118:261002
TITLE: Stable crystals of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine
INVENTOR(S): Sumikawa, Michito; Koguchi, Yoshihito; Ohgane, Takao; Irie, Yasuo; Takahashi, Satoji
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 526171	A2	19930203	EP 1992-306895	19920729
EP 526171	A3	19930505		
EP 526171	B1	19970305		
R: AT, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
JP 05208943	A	19930820	JP 1992-202686	19920729
JP 2508949	B2	19960619		
AT 149483	T	19970315	AT 1992-306895	19920729
ES 2100291	T3	19970616	ES 1992-306895	19920729
CA 2114678	A1	19950802	CA 1994-2114678	19940201
CA 2114678	C	19990427		
PRIORITY APPLN. INFO.:			JP 1991-189696 A	19910730
			JP 1991-199453 A	19910808

AB Stable H-type crystals of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (I) are obtained by treating I with a solvent, at >10°. A solution of 5 g I in 20 mL acetone was added to a stirred mixture of 40 mL acetone and 60 mL water, at 25° to precipitate H-type crystals. The crystals have different m.p., IR spectrum and x-ray diffraction patterns from known forms of I and are not converted to other forms when ground.

L4 ANSWER 44 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1989:458305 HCAPLUS
DOCUMENT NUMBER: 111:58305
TITLE: N-(Cyclohexylcarbonyl)-D-phenylalanines and related compounds. A new class of oral hypoglycemic agents. 2
AUTHOR(S): Shinkai, Hisashi; Nishikawa, Masahiko; Sato, Yusuke; Toi, Koji; Kumashiro, Izumi; Seto, Yoshiko; Fukuma, Mariko; Dan, Katsuaki; Toyoshima, Shigeshi
CORPORATE SOURCE: Cent. Res. Lab., Ajinomoto Co., Inc., Kawasaki, 210, Japan
SOURCE: Journal of Medicinal Chemistry (1989), 32(7), 1436-41
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 111:58305

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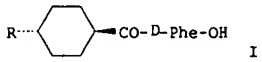

I

AB A series of analogs, e.g., I (R = alkyl, Ph), of N-(cyclohexylcarbonyl)-D-phenylalanine have been synthesized and evaluated for their hypoglycemic activity. Relationships were studied between the activity and the three-dimensional structure of the acyl moiety, which was characterized by high-resolution 1H NMR spectroscopy and MNDO calcns. The role of the carboxyl group of the phenylalanine moiety was also studied by comparing the activities of the enantiomers, the decarboxyl derivative, the esters, and the amides of the phenylalanine derivs. Thus, the structural requirements for possessing hypoglycemic activity was elucidated and a highly active compound, N-[(trans-4-isopropylcyclohexyl)carbonyl]-D-phenylalanine (I, R = CHMe2) was obtained, which showed a 20% blood glucose decrease at an oral dose of 1.6 mg/kg in fasted normal mice.

L4 ANSWER 45 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1987:85057 HCAPLUS
Correction of: 1987:19047
DOCUMENT NUMBER: 106:85057
Correction of: 106:19047
TITLE: Preparation of D-phenylalanine derivatives and their use as hypoglycemic agents
INVENTOR(S): Toyoshima, Shigeshi; Seto, Yoshiko; Shinkai, Hisashi; Toi, Koji; Kumashiro, Izumi
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: Eur. Pat. Appl., 25 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 196222	A2	19861001	EP 1986-302217	19860326
EP 196222	A3	19880224		
EP 196222	B1	19920129		
R: CH, DE, FR, GB, LI				
JP 63054321	A	19880308	JP 1986-61833	19860319
JP 04015221	B	19920317		
US 4816484	A	19890328	US 1988-146719	19880121
US 34878	E	19950314	US 1993-157564	19931123

PRIORITY APPLN. INFO.:
JP 1985-62276 A 19850327
JP 1986-38111 A1 19860222
US 1986-844970 A3 19860327
US 1988-146719 A5 19880121
US 1989-844970 B3 19890327

OTHER SOURCE(S): CASREACT 106:85057; MARPAT 106:85057
AB D-Phenylalanine derivs. D-R2CONR3CH(CO2R1)CH2Ph [I; R1 = H, C1-5 alkyl, C6-12 aryl or aralkyl, Q, CH2CO2R3, CHMeOCOR3, CH2OCOCMe3; R2 = (un)substituted C6-12 aryl, 5- or 6-membered heterocyclyl, cycloalkyl, cycloalkenyl; R3 = H, C1-5 alkyl], their salts. and precursors which can

be converted thereto in the human or animal body, useful as hypoglycemics, were prepared via conventional N-acylating reactions. D-Phenylalanine in 10% aqueous NaOH was successively treated with Me2CO, 4-EtC6H4COCl in Me2CO, and 10% aqueous NaOH to give 83% acylphenylanine D-II. At 25 mg/kg in mice, D-II decreased blood glucose 34% in min.

L4 ANSWER 46 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1987:19047 HCAPLUS
DOCUMENT NUMBER: 106:19047
TITLE: Preparation of D-phenylalanine derivatives and their use as hypoglycemic agents
INVENTOR(S): Toyoshima, Shigeshi; Seto, Yoshiko; Shinkai, Hisashi; Toi, Koji; Kumashiro, Izumi
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
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CODEN: EPXXDW
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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 196222 A2		19861001	EP 1986-302217	19860326
R: CH, DE, FR, GB, LI				

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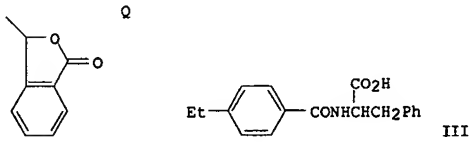

III

AB D-Phenylalanine derivs. D-R2CONR3CH(CO2R1)CH2Ph [I; R1 = H, C1-5 alkyl, C6-12 aryl or aralkyl, Q, CH2CO2R3, CHMeOCOR3, CH2OCOCMe3; R2 = (un)substituted C6-12 aryl, 5- or 6-membered heterocyclyl, cycloalkyl, cycloalkenyl; R3 = H, C1-5 alkyl], their salts, and precursors which can be converted thereto in the human or animal body, useful as hypoglycemics, were prepared via conventional N-acylating reactions. D-Phenylalanine in 10% aqueous NaOH was successively treated with Me2CO, 4-EtC6H4COCl in Me2CO, and 10% aqueous NaOH to give 83% acylphenylanine D-II. At 25 mg/kg in mice, D-II decreased blood glucose 34% in 60 min.